



Clinical trial results:

A phase III assessor-blinded randomised parallel group multi-centre study to compare efficacy and safety of two r-hFSH formulations (AFOLIA and Gonal-f®) in women for assisted reproductive treatment Summary

EudraCT number	2010-019287-37
Trial protocol	DE AT ES GB DK
Global end of trial date	31 December 2012

Results information

Result version number	v2 (current)
This version publication date	03 October 2020
First version publication date	04 March 2016
Version creation reason	<ul style="list-style-type: none">• New data added to full data set Final data based on CSR vers 2, 15 August 2019

Trial information

Trial identification

Sponsor protocol code	FIN3001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01121666
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Finox AG
Sponsor organisation address	Technikumstrasse 2, Burgdorf, Switzerland, 3401
Public contact	Julian Jenkins, Finox AG, +41 34 426 11 11, info@finoxbiotech.com
Scientific contact	Julian Jenkins, Finox AG, +41 34 426 11 11, info@finoxbiotech.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	15 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 April 2012
Global end of trial reached?	Yes
Global end of trial date	31 December 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate equivalence between AFOLIA and Gonal-f.

Protection of trial subjects:

Study Design:

This was a multi-centre, assessor-blind, comparative Phase III study with central patient randomisation. After obtaining informed consent, patients were screened for eligibility for the study. The endogenous follicle-stimulating hormone (FSH) production of eligible patients was down-regulated with a gonadotropin-releasing hormone (GnRH)-agonist. After down-regulation of endogenous FSH, patients were randomised 2:1 to receive either AFOLIA or Gonal-f daily. FSH in both groups was administered subcutaneously (s.c.). A starting dose of 150 IU/day was administered in both groups. Ovarian response was assessed by vaginal ultrasound on Days 1, 6, 8 after the start of FSH administration (Visits 3, 4 and 5), and on the day of human chorionic gonadotropin (hCG) application, 16 days after start of treatment with recombinant human follicle stimulating hormone (r-hFSH) at the latest. For patients' safety, serum estradiol (E2) concentration was also measured. After Day 8 assessment, follicular development was monitored by vaginal ultrasound at an interval of 2-3 days. Patients received daily r-hFSH until at least 1 follicle reached a diameter of ≥ 18 mm and 2 additional follicles reached a diameter of ≥ 16 mm, but no longer than 16 days. At this time, hCG was given to trigger ovulation. Oocytes were removed and intracytoplasmic sperm injection (ICSI) or in vitro fertilisation (IVF) was performed according to standard techniques. A maximum of 2 embryos were transferred 2 to 5 days after oocyte retrieval (OR). Pregnancy rate was determined biochemically and clinically.

Criteria for Safety Evaluation:

- Adverse events
- Local and systemic adverse event pattern (incl. ovarian hyper stimulation syndrome (OHSS))
- Time to first Onset of OHSS
- Time to first Dose Reduction due to imminent OHSS
- Percentage of patients with dose reduction due to imminent OHSS
- Clinical laboratory tests
- Vital signs
- Physical examination / Health status

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 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	Spain: 52
Country: Number of subjects enrolled	United Kingdom: 31
Country: Number of subjects enrolled	Austria: 131

Country: Number of subjects enrolled	Denmark: 112
Country: Number of subjects enrolled	Germany: 35
Country: Number of subjects enrolled	Switzerland: 11
Worldwide total number of subjects	372
EEA total number of subjects	361

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)	372
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were screened and enrolled at 15 centers in six European countries from July 2010 until April 2012

Pre-assignment

Screening details:

Of 460 participants in this trial 88 were reported as screening failures prior the group assignment

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor ^[1]

Arms

Are arms mutually exclusive?	Yes
Arm title	AFOLIA-150 (Follitropin Alfa)

Arm description:

Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days

Arm type	Experimental
Investigational medicinal product name	AFOLIA-150 (Follitropin alfa)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

150IU per day subcutaneously for a maximum of 16 days

Arm title	Gonal-f® (Follitropin Alfa)
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Arm description:

Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days.

Arm type	Active comparator
Investigational medicinal product name	Gonal-f® (Follitropin alfa)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

150IU per day subcutaneously for a maximum of 16 days

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: The information is correct. This was a multi-centre, assessor-blind, comparative Phase III study with central patient randomisation.

Number of subjects in period 1	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)
Started	249	123
Completed	220	113
Not completed	29	10
Protocol deviation	29	10

Baseline characteristics

Reporting groups

Reporting group title	AFOLIA-150 (Follitropin Alfa)
Reporting group description:	
Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days	
Reporting group title	Gonal-f® (Follitropin Alfa)
Reporting group description:	
Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days.	

Reporting group values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	Total
Number of subjects	249	123	372
Age categorical			
Units: Subjects			
Adults (18-64 years)	249	123	372
Age continuous			
Units: years			
arithmetic mean	31.8	32.1	
standard deviation	± 4.02	± 3.76	-
Gender categorical			
Units: Subjects			
Female	249	123	372
Male	0	0	0
Race			
Units: Subjects			
Caucasian	229	117	346
Asian	12	3	15
Other	6	2	8
Black	2	1	3
FSH baseline concentration			
The FSH concentration was measured at baseline in IU/L.			
Units: IU/L			
arithmetic mean	6.9	6.9	
standard deviation	± 1.51	± 1.56	-
Antral follicle count			
Units: Antral follicle count			
arithmetic mean	15.1	15.3	
standard deviation	± 3.77	± 3.83	-
Body Mass Index			
Units: kilogram(s)/square meter			
arithmetic mean	22.7	22.4	
standard deviation	± 2.9	± 2.56	-
GnRH-agonist duration			
Units: days			
arithmetic mean	23.5	22.7	
standard deviation	± 7.89	± 7.46	-

Subject analysis sets

Subject analysis set title	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)
Subject analysis set type	Per protocol

Subject analysis set description:

Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days; Per Protocol Population

Subject analysis set title	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject analysis set type	Per protocol

Subject analysis set description:

Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days; Per Protocol Population

Subject analysis set title	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days; Population with a second treatment cycle

Subject analysis set title	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days; Population with a second treatment cycle

Reporting group values	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)
Number of subjects	220	113	72
Age categorical Units: Subjects			
Adults (18-64 years)	220	113	72
Age continuous Units: years			
arithmetic mean	31.9	32.2	32.2
standard deviation	± 4.03	± 3.65	± 3.66
Gender categorical Units: Subjects			
Female	220	113	72
Male	0	0	0
Race Units: Subjects			
Caucasian	202	109	64
Asian	2	1	4
Other	11	3	2
Black	2	0	2
FSH baseline concentration			
The FSH concentration was measured at baseline in IU/L.			
Units: IU/L			
arithmetic mean	6.9	6.8	7.0
standard deviation	± 1.37	± 1.52	± 1.29
Antral follicle count Units: Antral follicle count			
arithmetic mean	15.1	15.3	15.2
standard deviation	± 3.77	± 3.79	± 4.62
Body Mass Index Units: kilogram(s)/square meter			

arithmetic mean	22.7	22.4	23.5
standard deviation	± 2.87	± 2.60	± 2.90
GnRH-agonist duration			
Units: days			
arithmetic mean	23.6	22.5	23.3
standard deviation	± 7.97	± 7.52	± 7.46

Reporting group values	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Number of subjects	38		
Age categorical			
Units: Subjects			
Adults (18-64 years)	38		
Age continuous			
Units: years			
arithmetic mean	31.6		
standard deviation	± 3.49		
Gender categorical			
Units: Subjects			
Female	38		
Male	0		
Race			
Units: Subjects			
Caucasian	35		
Asian	2		
Other	0		
Black	1		
FSH baseline concentration			
The FSH concentration was measured at baseline in IU/L.			
Units: IU/L			
arithmetic mean	7.1		
standard deviation	± 1.69		
Antral follicle count			
Units: Antral follicle count			
arithmetic mean	14.6		
standard deviation	± 4.04		
Body Mass Index			
Units: kilogram(s)/square meter			
arithmetic mean	22.6		
standard deviation	± 2.74		
GnRH-agonist duration			
Units: days			
arithmetic mean	22.0		
standard deviation	± 8.36		

End points

End points reporting groups

Reporting group title	AFOLIA-150 (Follitropin Alfa)
Reporting group description:	
Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days	
Reporting group title	Gonal-f® (Follitropin Alfa)
Reporting group description:	
Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days.	
Subject analysis set title	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)
Subject analysis set type	Per protocol
Subject analysis set description:	
Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days; Per Protocol Population	
Subject analysis set title	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject analysis set type	Per protocol
Subject analysis set description:	
Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days; Per Protocol Population	
Subject analysis set title	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days; Population with a second treatment cycle	
Subject analysis set title	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days; Population with a second treatment cycle	

Primary: Number of Oocytes Retrieved

End point title	Number of Oocytes Retrieved
End point description:	
As soon as ovulation criteria were reached, HCG was given to trigger ovulation and 34-36 hours later, oocytes were retrieved. If criteria for ovulation triggering could not be reached by FSH stimulation on day 16, treatment was to be stopped. The equivalence in the number of retrieved oocytes was tested using a pre-determined clinical equivalence margin of +/- 2.9 oocytes	
End point type	Primary
End point timeframe:	
34-36 hours after hCG administration and after maximum 16 days of r-hFSH treatment	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: Number of retrieved oocytes				
arithmetic mean (standard deviation)	10.7 (± 5.62)	10.4 (± 6.14)	10.8 (± 5.11)	10.6 (± 6.06)

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Number of retrieved oocytes				
arithmetic mean (standard deviation)	10.4 (± 4.21)	10.1 (± 5.28)		

Statistical analyses

Statistical analysis title	Number of Oocytes Retrieved (Per Protocol Pop.)
Statistical analysis description:	
This study was powered to test equivalence using a two one-sided test (TOST) of the number of oocytes retrieved.	
Comparison groups	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population) v Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Number of subjects included in analysis	333
Analysis specification	Pre-specified
Analysis type	equivalence ^[1]
P-value	= 0.0003 ^[2]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - This study was powered to test equivalence using a two one-sided test (TOST) of the number of oocytes retrieved with a power of 90%, an alpha error of 2.5% and a pre-determined clinical equivalence margin of +/-2.9 oocytes for the relevant population.

[2] - This study was powered to test equivalence using a two one-sided test (TOST) with a power of 90%, an alpha error of 2.5% and a pre-determined clinical equivalence margin of +/-2.9 oocytes for the relevant population.

Statistical analysis title	Number of Oocytes Retrieved (Cycle 2)
Comparison groups	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle) v Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0257
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Number of Oocytes Retrieved (Reporting group)
Comparison groups	Gonal-f® (Follitropin Alfa) v AFOLIA-150 (Follitropin Alfa)

Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0003
Method	Wilcoxon (Mann-Whitney)

Secondary: E2 Concentration at Day 8 and at Day of hCG Administration

End point title	E2 Concentration at Day 8 and at Day of hCG Administration
End point description:	The serum concentration of oestradiol was assessed at day 8 and the day of hCG administration.
End point type	Secondary
End point timeframe:	Day 8 of stimulation and at the day of hCG administration (after max. 16 days of r-FSH treatment)

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: pmol/L				
arithmetic mean (standard deviation)				
Day of hCG administration	8982.3 (± 6535.3)	7704.2 (± 5345.8)	9019.6 (± 6622.4)	7928.4 (± 5349.9)
Day 8	3958.9 (± 3699.4)	3234 (± 2428.1)	3849.7 (± 3607.0)	3184.8 (± 2422.3)

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed				
Units: pmol/L				
arithmetic mean (standard deviation)				
Day of hCG administration	8405.3 (± 4591.8)	8426.5 (± 5821.7)		
Day 8	3220.0 (± 2733.9)	3226.0 (± 2975.7)		

Statistical analyses

Secondary: Total Dose of r-hFSH Administered

End point title	Total Dose of r-hFSH Administered
End point description:	Total dose of r-hFSH required was assessed.
End point type	Secondary
End point timeframe:	Day of hCG administration (after maximum 16 days of r-hFSH treatment)

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	249	123	72	38
Units: Mean total dose of r-hFSH (IU)				
arithmetic mean (standard deviation)	1555.7 (± 293)	1569.2 (± 259.2)	1612.3 (± 212.67)	1604.9 (± 216.61)

Statistical analyses

Statistical analysis title	Total Dose of r-hFSH Administered
Comparison groups	AFOLIA-150 (Follitropin Alfa) v Gonal-f® (Follitropin Alfa)
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9638
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Total Dose of r-hFSH Administered (2nd cycle)
Comparison groups	Gonal-f® (Follitropin Alfa) (2nd treatment cycle) v AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8637
Method	Wilcoxon (Mann-Whitney)

Secondary: Quality of Oocytes Retrieved (Day 2+3)

End point title	Quality of Oocytes Retrieved (Day 2+3)
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End point description:	
Number of patients with ovum pick-up	
End point type	Secondary
End point timeframe:	
34-36 hours after hCG administration	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	72	38
Units: Participants				
Day 2	82	36	30	17
Day 3	53	28	15	12

Statistical analyses

No statistical analyses for this end point

Secondary: Fertilisation Rate of Oocytes

End point title	Fertilisation Rate of Oocytes
End point description:	
Fertilisation rate was assessed	
End point type	Secondary
End point timeframe:	
1 day after ovum pick-up	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: Participants				
arithmetic mean (standard deviation)	66.1 (± 24.84)	64 (± 24.76)	65.7 (± 25.12)	64.1 (± 25.06)

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
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Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Participants				
arithmetic mean (standard deviation)	66.0 (\pm 31.34)	66.37 (\pm 27.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Embryo Quality: Mean Number of Blastomeres

End point title	Embryo Quality: Mean Number of Blastomeres
End point description:	
Main embryo quality parameter "mean number of blastomeres"	
End point type	Secondary
End point timeframe:	
Day 2 of OPU/fertilisation	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	72	38
Units: Number of blastomeres at day 3				
arithmetic mean (standard deviation)	6.6 (\pm 2.41)	6.4 (\pm 2.49)	6.2 (\pm 2.14)	6.8 (\pm 2.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Cryopreserved 2PNs, Embryos/Blastocysts

End point title	Number of Cryopreserved 2PNs, Embryos/Blastocysts
End point description:	
End point type	Secondary
End point timeframe:	
Day 1, 2, 3 and 5 of OPU/fertilisation	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: Patients with cryopreservation	103	55	91	50

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Patients with cryopreservation	28	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days of r-hFSH Stimulation

End point title	Number of Days of r-hFSH Stimulation
End point description: Mean duration of stimulation was assessed.	
End point type	Secondary
End point timeframe: At the day of hCG administration	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	249	123	72	38
Units: Duration of FSH medication (days)				
arithmetic mean (standard deviation)	10.6 (± 1.91)	10.7 (± 1.72)	10.9 (± 1.33)	10.9 (± 1.31)

Statistical analyses

Statistical analysis title	Number of Days of r-hFSH Stimulation
Comparison groups	AFOLIA-150 (Follitropin Alfa) v Gonal-f® (Follitropin Alfa)

Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8926
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Number of Days of r-hFSH Stimulation (2nd cycle)
Comparison groups	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle) v Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9613
Method	Wilcoxon (Mann-Whitney)

Secondary: Number of Patients With Cycle Cancellation

End point title	Number of Patients With Cycle Cancellation
End point description:	Number of patients with cycle cancellation was assessed.
End point type	Secondary
End point timeframe:	At the end of the study

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	72	38
Units: Cycle cancellations	13	5	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Patients With Good Response

End point title	Number of Patients With Good Response
End point description:	Good response was defined as "patients with an oocyte retrieval of four or more oocytes"
End point type	Secondary

End point timeframe:
At the end of the study

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	249	123	72	38
Units: Participants	217	107	67	33

Statistical analyses

No statistical analyses for this end point

Secondary: Implantation Rate

End point title	Implantation Rate
End point description: Defined as fetal sac per embryo transferred.	
End point type	Secondary
End point timeframe: Five to six weeks after oocyte retrieval	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	249	123	72	38
Units: Percentage of implantations number (not applicable)	31.8	36.7	28.7	21.1

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Pregnancy Rate

End point title	Clinical Pregnancy Rate
End point description: Presence of at least one intrauterine gestational sac.	
End point type	Secondary

End point timeframe:

Five to six weeks after oocyte retrieval

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: Clinical pregnancies	90	55	83	51

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Clinical pregnancies	25	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Ongoing Pregnancy

End point title	Ongoing Pregnancy
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End point description:

Ongoing pregnancy per embryo transfer. Presence of at least one viable fetus 10 weeks after embryo transfer.

End point type	Secondary
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End point timeframe:

Ten weeks after embryo transfer

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: Ongoing pregnancies	84	51	78	48

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Ongoing pregnancies	22	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Live Birth Rate

End point title	Live Birth Rate
End point description:	
Patients with liveborn children	
End point type	Secondary
End point timeframe:	
After childbirth with questionnaire	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: Patients with liveborn children	80	50	74	47

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Patients with liveborn children	22	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Embryo Quality: Absence of Multinucleation

End point title Embryo Quality: Absence of Multinucleation

End point description:

Main embryo quality parameter "absence of multinucleation" observed.

End point type Secondary

End point timeframe:

Day 3

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	249	123	72	38
Units: Percentage of absent multinucleation				
number (not applicable)	93.6	93.9	97.9	91.7

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Oocytes Retrieved (Day 4+5)

End point title Quality of Oocytes Retrieved (Day 4+5)

End point description:

Number of patients with transferred blastocysts

End point type Secondary

End point timeframe:

At day 4 and 5

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246	123		
Units: Participants				
Day 4	10	2		
Day 5	76	46		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Oocytes Retrieved (transfer day)

End point title	Quality of Oocytes Retrieved (transfer day)
End point description: Number of embryos per blastocysts transferred	
End point type	Secondary
End point timeframe: Day of transfer	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	249	123	220	113
Units: Embryos per blastocysts transferred				
arithmetic mean (standard deviation)	1.5 (± 0.52)	1.6 (± 0.53)	1.5 (± 0.52)	1.5 (± 0.52)

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Embryos per blastocysts transferred				
arithmetic mean (standard deviation)	1.7 (± 0.51)	1.6 (± 0.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Oocytes Retrieved (CO Maturity)

End point title	Quality of Oocytes Retrieved (CO Maturity)
End point description: The maturity of the cumulus oophorus was assessed.	
End point type	Secondary
End point timeframe: After oocyte retrieval	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: Percentage of cumulus oophori				
number (not applicable)				
very mature	9.1	9.4	8.4	9.1
mature	75.7	75.3	76.1	76.2
immature	14.5	14.2	14.7	13.5

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Percentage of cumulus oophori				
number (not applicable)				
very mature	3.7	5.2		
mature	79.4	79.4		
immature	14.3	15.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Oocytes Retrieved (Nuclear Maturity)

End point title	Quality of Oocytes Retrieved (Nuclear Maturity)
End point description:	The nuclear maturity was assessed (Germinal vesicle, Metaphase I, Metaphase II).
End point type	Secondary
End point timeframe:	
After oocyte retrieval	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: Percentage of cells				
number (not applicable)				
Germinal vesicle	9.5	9.1	10.0	9.1
Metaphase I	7.2	7.7	7.6	7.3
Metaphase II	83.4	83.3	82.4	83.6

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Percentage of cells				
number (not applicable)				
Germinal vesicle	10.5	6.1		
Metaphase I	8.2	8.6		
Metaphase II	81.3	85.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number and Size of Follicles at the Day of hCG administration

End point title Number and Size of Follicles at the Day of hCG administration

End point description:

The number and size of follicles at day of hCG administration were evaluated as secondary end-point.

End point type Secondary

End point timeframe:

Day of hCG administration (after maximum 16 days of r-hFSH treatment)

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: Number of follicles				
arithmetic mean (standard deviation)				

≥ 12 mm	11.8 (± 4.73)	11.1 (± 4.23)	11.8 (± 4.33)	11.2 (± 4.12)
≥ 15 mm	8.3 (± 3.81)	7.7 (± 3.60)	8.2 (± 3.62)	7.8 (± 3.49)
≥ 17 mm	4.9 (± 3.29)	4.5 (± 2.71)	4.9 (± 3.25)	4.6 (± 2.74)

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Number of follicles				
arithmetic mean (standard deviation)				
≥ 12 mm	11.4 (± 3.96)	11.4 (± 4.11)		
≥ 15 mm	8.0 (± 3.20)	7.7 (± 3.52)		
≥ 17 mm	4.5 (± 2.97)	4.2 (± 3.41)		

Statistical analyses

Statistical analysis title	Number/Size of Follicles 12 mm
Comparison groups	AFOLIA-150 (Follitropin Alfa) v Gonal-f® (Follitropin Alfa)
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	other ^[3]
P-value	= 0.2357
Method	Wilcoxon (Mann-Whitney)

Notes:

[3] - Follicles of 12 mm

Statistical analysis title	Number/Size of Follicles 15 mm
Comparison groups	AFOLIA-150 (Follitropin Alfa) v Gonal-f® (Follitropin Alfa)
Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1395
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Number/Size of Follicles 17 mm
Comparison groups	AFOLIA-150 (Follitropin Alfa) v Gonal-f® (Follitropin Alfa)

Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3992
Method	Wilcoxon (Mann-Whitney)

Secondary: Number and Size of Follicles ≥ 12 mm at Day 8 of Stimulation

End point title	Number and Size of Follicles ≥ 12 mm at Day 8 of Stimulation
End point description:	
End point type	Secondary
End point timeframe:	
Day 8 of Stimulation	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Per Protocol Population)	Gonal-f® (Follitropin Alfa) (Per Protocol Population)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	220	113
Units: Numbers of follicles				
arithmetic mean (standard deviation)				
≥ 12 mm	7.1 (\pm 5.11)	6.5 (\pm 4.65)	6.9 (\pm 4.86)	6.5 (\pm 4.60)

End point values	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	38		
Units: Numbers of follicles				
arithmetic mean (standard deviation)				
≥ 12 mm	5.8 (\pm 3.79)	5.9 (\pm 4.08)		

Statistical analyses

Statistical analysis title	Number/Size of Follicles 12 mm
Comparison groups	AFOLIA-150 (Follitropin Alfa) v Gonal-f® (Follitropin Alfa)

Number of subjects included in analysis	369
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3434
Method	Wilcoxon (Mann-Whitney)

Secondary: Safety - patients with dose reduction due to imminent OHSS

End point title	Safety - patients with dose reduction due to imminent OHSS
End point description:	
End point type	Secondary
End point timeframe:	
During the study	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	246	123	72	38
Units: Number of patients	26	9	3	2

Statistical analyses

No statistical analyses for this end point

Secondary: Safety - Number of Patients with OHSS event

End point title	Safety - Number of Patients with OHSS event
End point description:	
Number of patients with at least 1 OHSS event	
End point type	Secondary
End point timeframe:	
During the study	

End point values	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (2nd treatment cycle)	Gonal-f® (Follitropin Alfa) (2nd treatment cycle)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	249	123	72	38
Units: Number of patients	55	16	5	2

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Study period plus 30 days

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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Reporting groups

Reporting group title	AFOLIA-150 (Follitropin Alfa)
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Reporting group description:

Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days

Reporting group title	Gonal-f® (Follitropin Alfa)
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Reporting group description:

Follitropin alfa: 150IU per day subcutaneously for a maximum of 16 days.

Reporting group title	AFOLIA-150 (Follitropin Alfa) (Cycle 2)
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Reporting group description: -

Reporting group title	Gonal-f® (Follitropin Alfa) (Cycle 2)
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Reporting group description: -

Serious adverse events	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Cycle 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 249 (4.42%)	3 / 123 (2.44%)	0 / 72 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Body temperature increased			
subjects affected / exposed	1 / 249 (0.40%)	0 / 123 (0.00%)	0 / 72 (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
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 249 (0.00%)	1 / 123 (0.81%)	0 / 72 (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
Reproductive system and breast disorders			
Ovarian hyperstimulation syndrome			

subjects affected / exposed	7 / 249 (2.81%)	2 / 123 (1.63%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	7 / 7	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian haemorrhage			
subjects affected / exposed	1 / 249 (0.40%)	0 / 123 (0.00%)	0 / 72 (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			
subjects affected / exposed	2 / 249 (0.80%)	0 / 123 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 249 (0.40%)	0 / 123 (0.00%)	0 / 72 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Gonal-f® (Follitropin Alfa) (Cycle 2)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 38 (2.63%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Body temperature increased			
subjects affected / exposed	0 / 38 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 38 (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	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian haemorrhage			
subjects affected / exposed	0 / 38 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 38 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 38 (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	AFOLIA-150 (Follitropin Alfa)	Gonal-f® (Follitropin Alfa)	AFOLIA-150 (Follitropin Alfa) (Cycle 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	182 / 249 (73.09%)	83 / 123 (67.48%)	46 / 72 (63.89%)
Nervous system disorders			
Headache			
subjects affected / exposed	55 / 249 (22.09%)	25 / 123 (20.33%)	13 / 72 (18.06%)
occurrences (all)	55	25	13
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	68 / 249 (27.31%)	44 / 123 (35.77%)	20 / 72 (27.78%)
occurrences (all)	68	44	20
Injection site haematoma			
subjects affected / exposed	60 / 249 (24.10%)	19 / 123 (15.45%)	15 / 72 (20.83%)
occurrences (all)	60	19	15
Injection site pain			

subjects affected / exposed occurrences (all)	39 / 249 (15.66%) 39	21 / 123 (17.07%) 21	6 / 72 (8.33%) 6
Injection site swelling subjects affected / exposed occurrences (all)	15 / 249 (6.02%) 15	10 / 123 (8.13%) 10	6 / 72 (8.33%) 6
Fatigue subjects affected / exposed occurrences (all)	13 / 249 (5.22%) 13	4 / 123 (3.25%) 4	3 / 72 (4.17%) 3
Haemorrhage subjects affected / exposed occurrences (all)	2 / 249 (0.80%) 2	2 / 123 (1.63%) 2	0 / 72 (0.00%) 0
Reproductive system and breast disorders Ovarian hyperstimulation syndrome subjects affected / exposed occurrences (all)	55 / 249 (22.09%) 55	16 / 123 (13.01%) 16	5 / 72 (6.94%) 5
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	23 / 249 (9.24%) 23	6 / 123 (4.88%) 6	5 / 72 (6.94%) 5
Abdominal distension subjects affected / exposed occurrences (all)	14 / 249 (5.62%) 14	6 / 123 (4.88%) 6	3 / 72 (4.17%) 3
Abdominal pain subjects affected / exposed occurrences (all)	13 / 249 (5.22%) 13	6 / 123 (4.88%) 6	2 / 72 (2.78%) 2
Abdominal pain upper subjects affected / exposed occurrences (all)	7 / 249 (2.81%) 7	7 / 123 (5.69%) 7	0 / 72 (0.00%) 0
Abdominal pain lower subjects affected / exposed occurrences (all)	11 / 249 (4.42%) 11	2 / 123 (1.63%) 2	0 / 72 (0.00%) 0
Non-serious adverse events	Gonal-f® (Follitropin Alfa) (Cycle 2)		
Total subjects affected by non-serious adverse events subjects affected / exposed	28 / 38 (73.68%)		

Nervous system disorders			
Headache			
subjects affected / exposed	10 / 38 (26.32%)		
occurrences (all)	10		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	16 / 38 (42.11%)		
occurrences (all)	16		
Injection site haematoma			
subjects affected / exposed	14 / 38 (36.84%)		
occurrences (all)	14		
Injection site pain			
subjects affected / exposed	8 / 38 (21.05%)		
occurrences (all)	8		
Injection site swelling			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences (all)	1		
Haemorrhage			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Ovarian hyperstimulation syndrome			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	2		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences (all)	1		
Abdominal distension			
subjects affected / exposed	4 / 38 (10.53%)		
occurrences (all)	4		
Abdominal pain			

subjects affected / exposed	3 / 38 (7.89%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences (all)	1		
Abdominal pain lower			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences (all)	2		

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

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25735918>