ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 01/20/2014

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Study Identification

Unique Protocol ID:	28613
Brief Title:	CONSORT Randomized Controlled Trial in Assisted Reproductive Technology
Official Title:	A Phase IV Prospective, Multicenter, Randomized, Open-label Trial to Assess the Efficacy and Safety of GONAL f® at a Dose Based on Subject Baseline Characteristics Determined According to the CONSORT Calculator Compared With a Standard Dose of GONAL f® 150 IU Per Day for Ovarian Stimulation in Women Undergoing Assisted Reproductive Technology (ART)
Secondary IDs:	

Study Status

Record Verification:	January 2014
Overall Status:	Completed
Study Start:	August 2008
Primary Completion:	January 2010 [Actual]
Study Completion:	January 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Merck KGaA
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	No

IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 14Aug08 Board Name: Region Nordjylland Videnskabsetsik Komité Board Affiliation: Independent Phone: 963-51000 Email: region@rn.dk
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Australia: Human Research Ethics Committee Chile: Comisión Nacional de Investigación Científica y Tecnológica Chile: Instituto de Salud Pública de Chile Denmark: Danish Dataprotection Agency Denmark: Danish Medicines Agency Denmark: The Regional Committee on Biomedical Research Ethics France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) France: Institutional Ethical Committee France: National Consultative Ethics Committee for Health and Life Sciences Germany: Ethics Commission Germany: Federal Institute for Drugs and Medical Devices Italy: Ethics Committee Italy: National Monitoring Center for Clinical Trials - Ministry of Health Netherlands: Medical Ethics Review Committee (METC) Netherlands: The Central Committee on Research Involving Human Subjects (CCMO) Spain: Comité Ético de Investigación Clínica Spain: Spanish Agency of Medicines Sweden: Medical Products Agency Sweden: Regional Ethical Review Board Switzerland: Ethikkommission Switzerland: Swissmedic United Kingdom: Medicines and Healthcare Products Regulatory Agency United Kingdom: Research Ethics Committee

Study Description

Brief Summary:	The overall objective of this trial is to compare the ovarian response in assisted reproductive technology (ART) subjects administered GONAL f® according to the 'Consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment' (CONSORT) calculator versus given a standard GONAL f® dose of 150 International Unit (IU) per day.
Detailed Description:	

Conditions

Conditions:	Infertility
Keywords:	Infertility Assisted reproductive technology

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	200 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: CONSORT Dosing GONAL-f® dose based on subject baseline characteristics determined according to the CONSORT calculator	Drug: GONAL f® prefilled pen GONAL f® doses starting at minimum of 112.5 IU per day and a maximum of 450 IU per day for 1 cycle only Other Names: • Follitropin alfa • Recombinant human follicle stimulating hormone (r-hFSH) • GONAL-f® Prefilled Pen
Active Comparator: Standard Dosing GONAL-f® at a standard dose of 150 IU per day	Drug: GONAL f® prefilled pen GONAL f® standard treatment arm (150 IU of GONAL f® per day) up to Day 5 of stimulation after which the dose can be adjusted based upon the subject's ovarian response and according to the center's standard practice. Other Names: • Follitropin alfa

Arms	Assigned Interventions
	• r-hFSH • GONAL-f® Prefilled Pen

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 34 Years

Gender: Female

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

1. Female subjects justifying an in-vitro fertilization (IVF)/embryo transfer (ET) treatment
2. Have a male partner with semen analysis within the past 6 months prior to randomization considered adequate to proceed with regular insemination or intracytoplasmic sperm injection (ICSI) according to the center's standard practice. If these criteria are not met, the subject can only be entered if donor sperm will be used
3. Between her 18th and 35th birthday (35 not included) at the time of the randomization visit
4. Body mass index (BMI) lower than 30 kilogram per square meter (kg/m^2) where the BMI is calculated according to the formula
5. Have a regular spontaneous ovulatory menstrual cycle between 21 and 35 days in length
6. Have an early follicular phase (Day 2-4) serum level of basal FSH lower than or equal to 12 International Unit per Liter (IU/L) measured in the center's local laboratory during the screening period (i.e. within 2 months prior to down-regulation start)
7. Presence of both ovaries
8. Normal uterine cavity, which in the investigator's opinion is compatible with pregnancy
9. Have a negative cervical papanicolaou (PAP) test within the last 6 months prior to randomization
10. Have at least 1 wash-out cycle (defined as greater than or equal to 30 days since the last dose of clomiphene citrate or gonadotrophin treatment) since the last ART cycle and/or clomiphene citrate or gonadotrophin treatment prior to starting gonadotropin releasing hormone (GnRH) agonist therapy
11. Willing and able to comply with the protocol for the duration of the trial
12. Have given written informed consent, prior to any trial-related procedure not part of normal medical care, with the understanding that consent may be withdrawn by the subject at any time without prejudice to her future medical care

Exclusion Criteria:

1. Have greater than or equal to 2 previous ART cycles with a poor response to gonadotrophin stimulation (defined as lower than or equal to 5 mature follicles and/or lower than or equal to 3 oocytes collected) or have greater than or equal to 2 previous ART cycles with a hyper response (defined as greater than or equal to 25 oocytes retrieved)

2. Any medical condition, which in the judgment of the investigator may interfere with the absorption, distribution, metabolism or excretion of the drug. In case of doubt, the subject in question should be discussed with Merck Serono's Medical responsible
3. Have previous severe ovarian hyperstimulation syndrome (OHSS)
4. Polycystic ovary syndrome (PCOS; Rotterdam criteria) to reduce the risk of the occurrence of OHSS
5. Presence of endometriosis requiring treatment
6. Uterine myoma requiring treatment
7. Any contraindication to being pregnant and/or carrying a pregnancy to term
8. Extra-uterine pregnancy within the last 3 months prior to screening
9. History of 3 or more miscarriages (early or late miscarriages) due to any cause
10. Tumors of the hypothalamus and pituitary gland
11. Ovarian enlargement or cyst of unknown etiology
12. Ovarian, uterine or mammary cancer
13. A clinically significant systemic disease
14. Known infection with Human Immunodeficiency Virus (HIV), Hepatitis B or C virus in the trial subject or her male partner,
15. Abnormal gynecological bleeding of undetermined origin
16. Known allergy or hypersensitivity to human gonadotrophin preparations,
17. Any active substance abuse or history of drug medication or alcohol abuse in the past 5 years prior to the screening visit
18. Entered previously into this trial or simultaneous participation in another clinical trial

Contacts/Locations

Study Officials: Pablo Arriagada, MD
Study Director
Merck Serono S.A. - Geneva

Locations: Switzerland
Research Site
Geneva, Switzerland

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Recruitment Details	Participants were enrolled at 22 clinical trial centers in 9 European countries and 1 center in Chile. Recruitment period: 29 August 2008 to 21 January 2010.
Pre-Assignment Details	A total of 244 participants gave informed consent and were screened for study entry. Forty-four (44) of these participants were not randomized due to: screening failure (38), failure to down regulate (3), or other reasons (3). A total of 200 participants were randomized to one of the two treatment arms.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Overall Study

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Started	96	104
Completed	82	83
Not Completed	14	21
Adverse Event	1	3
Protocol Violation	1	0
Lack of ovarian response to stimulation	9	5
Ovarian hyperstimulation syndrome (OHSS)	1	6
No fertilization	2	2
All embryos discarded	0	3
No embryo cleavage	0	2

Baseline Characteristics

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Baseline Measures

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment	Total
Number of Participants	96	104	200
Age, Categorical [units: participants]			
<=18 years	0	0	0
Between 18 and 65 years	96	104	200
>=65 years	0	0	0
Age, Continuous [1] [units: years] Mean (Standard Deviation)	30.0 (2.9)	30.6 (2.6)	30.3 (2.8)
Gender, Male/Female [units: participants]			
Female	96	104	200
Male	0	0	0
Region of Enrollment [units: participants]			
Chile	7	8	15
Denmark	26	26	52
France	6	5	11
Germany	13	16	29
Italy	10	10	20

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment	Total
Netherlands	5	6	11
Spain	4	6	10
Sweden	8	7	15
Switzerland	11	14	25
United Kingdom	6	6	12
Serum Anti-Mullerian Hormone (AMH) [1] [units: nanogram/milliliter (ng/mL)] Mean (Standard Deviation)	2.705 (1.870)	2.399 (1.492)	2.551 (1.692)
Serum Progesterone (P4) [1] [units: nanomole/liter (nmol/L)] Mean (Standard Deviation)	2.934 (2.328)	2.803 (2.291)	2.868 (2.303)

[1] Number of participants analyzed (N) = 86 and 93 for GONAL-f® CONSORT calculator and GONAL-f® standard treatment arm group respectively at screening.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Number of Oocytes Retrieved Per Participant
Measure Description	Mean number of oocytes retrieved on the day of ovum pick up (OPU) was calculated. Oocyte retrieval is a technique used in in-vitro fertilization in order to remove oocytes from the ovary of the female, enabling fertilization outside the body.
Time Frame	34-38 hours post-recombinant human choriogonadotropin (hCG) (OPU)
Safety Issue?	No

Analysis Population Description

The modified Intention-To-Treat (ITT) population included all participants randomized into trial who received at least 1 dose of GONAL-f®, and who completed primary efficacy assessment (total number of oocytes retrieved per participant following GONAL-f® stimulation and hCG injection). Participants were analyzed based on treatment they received.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	86	93
Number of Oocytes Retrieved Per Participant [units: oocytes] Mean (Standard Deviation)	10.0 (5.6)	11.8 (5.3)

Statistical Analysis 1 for Number of Oocytes Retrieved Per Participant

Statistical Analysis Overview	Comparison Groups	GONAL-f ® CONSORT Calculator, GONAL-f ® Standard Treatment
	Comments	The null hypothesis was that the difference between the mean number of oocytes [CONSORT calculator dosing – Standard dosing] was less than or equal to [=<] (-3). The alternate hypothesis was that the difference was greater than [>] (-3).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.037
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.7
	Confidence Interval	(2-Sided) 95% -3.3 to -0.1

	Parameter Dispersion	Type: Standard Error of the mean Value: 0.8
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Total GONAL-f® Dose
Measure Description	
Time Frame	Start of treatment until end of stimulation cycle (approximately 28 days)
Safety Issue?	No

Analysis Population Description

The modified ITT population included all participants randomized into trial who received at least 1 dose of GONAL-f®, and who completed primary efficacy assessment (total number of oocytes retrieved per participant following GONAL-f® stimulation and hCG injection). Participants were analyzed based on treatment they received.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	86	93
Total GONAL-f® Dose [units: IU] Mean (Standard Deviation)	1288.54 (300.95)	1809.95 (546.90)

Statistical Analysis 1 for Total GONAL-f® Dose

Statistical Analysis Overview	Comparison Groups	GONAL-f ® CONSORT Calculator, GONAL-f ® Standard Treatment
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-511.37
	Confidence Interval	(2-Sided) 95% -638.78 to -383.96
	Parameter Dispersion	Type: Standard Error of the mean Value: 64.52
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Mean GONAL-f® Daily Dose
Measure Description	
Time Frame	Start of treatment until end of stimulation cycle (approximately 28 days)
Safety Issue?	No

Analysis Population Description

The modified ITT population included all participants randomized into trial who received at least 1 dose of GONAL-f®, and who completed primary efficacy assessment (total number of oocytes retrieved per participant following GONAL-f® stimulation and hCG injection). Participants were analyzed based on treatment they received.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.

	Description
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	86	93
Mean GONAL-f® Daily Dose [units: IU] Mean (Standard Deviation)	121.49 (22.56)	167.43 (30.79)

Statistical Analysis 1 for Mean GONAL-f® Daily Dose

Statistical Analysis Overview	Comparison Groups	GONAL-f ® CONSORT Calculator, GONAL-f ® Standard Treatment
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-45.60
	Confidence Interval	(2-Sided) 95% -53.75 to -37.46
	Parameter Dispersion	Type: Standard Error of the mean Value: 4.12
	Estimation Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Total Number of GONAL-f® Stimulation Treatment Days
Measure Description	
Time Frame	Start of treatment until end of stimulation cycle (approximately 28 days)
Safety Issue?	No

Analysis Population Description

The modified ITT population included all participants randomized into trial who received at least 1 dose of GONAL-f®, and who completed primary efficacy assessment (total number of oocytes retrieved per participant following GONAL-f® stimulation and hCG injection). Participants were analyzed based on treatment they received.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	86	93
Total Number of GONAL-f® Stimulation Treatment Days [units: days] Mean (Standard Deviation)	10.6 (1.7)	10.7 (1.6)

Statistical Analysis 1 for Total Number of GONAL-f® Stimulation Treatment Days

Statistical Analysis Overview	Comparison Groups	GONAL-f ® CONSORT Calculator, GONAL-f ® Standard Treatment
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.933
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.0
	Confidence Interval	(2-Sided) 95% -0.4 to 0.5
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.2
	Estimation Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Number of Participants With Cancelled Cycles Due to Excessive or Inadequate Response to Treatment
Measure Description	Number of participants with cancelled cycles due to excessive or inadequate response was evaluated. An excessive response: greater than or equal to 25 oocytes which could put the participant at risk of OHSS; An inadequate response: defined as 3 or less follicles of greater than or equal to 12 millimeter (mm) developing following at least 7 days of GONAL-f® treatment.
Time Frame	Start of treatment until Day 15-20 post-hCG
Safety Issue?	No

Analysis Population Description

All the randomized participants were analyzed for this outcome measure (N=200).

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	96	104
Number of Participants With Cancelled Cycles Due to Excessive or Inadequate Response to Treatment [units: Participants]		
Inadequate response	9	5
Excessive response (Risk of OHSS)	1	6

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Biochemical Pregnancies
Measure Description	Biochemical pregnancy was defined as a pregnancy diagnosed only by the detection of hCG in serum and that does not develop into a clinical pregnancy.
Time Frame	Start of treatment until Day 15-20 Post-hCG
Safety Issue?	No

Analysis Population Description

The modified ITT population included all participants randomized into trial who received at least 1 dose of GONAL-f®, and who completed primary efficacy assessment (total number of oocytes retrieved per participant following GONAL-f® stimulation and hCG injection). Participants were analyzed based on treatment they received.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	86	93

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Percentage of Participants With Biochemical Pregnancies [units: percentage of participants]	47.7	44.1

Statistical Analysis 1 for Percentage of Participants With Biochemical Pregnancies

Statistical Analysis Overview	Comparison Groups	GONAL-f ® CONSORT Calculator, GONAL-f ® Standard Treatment
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Percent difference]
	Estimated Value	3.6
	Confidence Interval	(2-Sided) 95% -11.0 to 18.2
	Estimation Comments	[Not specified]

7. Secondary Outcome Measure:

Measure Title	Number of Participants With Fetal Sacs and Fetal Hearts
Measure Description	Number of participants with fetal sacs and fetal hearts (with activity) as seen on an ultrasound scan to confirm clinical pregnancy.
Time Frame	Day 35-42 Post-hCG
Safety Issue?	No

Analysis Population Description

The modified ITT population included all participants randomized into trial who received at least 1 dose of GONAL-f®, and who completed primary efficacy assessment (total number of oocytes retrieved per participant following GONAL-f® stimulation and hCG injection). Participants were analyzed based on treatment they received.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	86	93
Number of Participants With Fetal Sacs and Fetal Hearts [units: participants]		
Missing (fetal sacs and fetal hearts)	47	57
0 (fetal sacs)	6	1
1 (fetal sacs)	27	25
2 (fetal sacs)	5	10
3 (fetal sacs)	1	0
0 (fetal hearts)	8	3
1 (fetal hearts)	25	24
2 (fetal hearts)	5	9
3 (fetal hearts)	1	0

8. Secondary Outcome Measure:

Measure Title	Implantation Rate
Measure Description	Implantation rate was measured as the number of gestational sacs observed divided by the number of embryos transferred multiplied by 100.
Time Frame	Day 35-42 Post-hCG

Safety Issue?	No

Analysis Population Description

The modified ITT population included all participants randomized into trial who received at least 1 dose of GONAL-f®, and who completed primary efficacy assessment (total number of oocytes retrieved per participant following GONAL-f® stimulation and hCG injection). Participants were analyzed based on treatment they received.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	86	93
Implantation Rate [units: percent sacs per embryo] Mean (Standard Deviation)	31.1 (41.3)	31.2 (40.8)

Statistical Analysis 1 for Implantation Rate

Statistical Analysis Overview	Comparison Groups	GONAL-f ® CONSORT Calculator, GONAL-f ® Standard Treatment
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.926
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.6
	Confidence Interval	(2-Sided) 95% -12.3 to 13.6
	Parameter Dispersion	Type: Standard Error of the mean Value: 6.6
	Estimation Comments	[Not specified]

9. Secondary Outcome Measure:

Measure Title	Number of Participants With Multiple Pregnancies
Measure Description	Multiple pregnancy was defined as 2 or more fetal hearts with activity.
Time Frame	Day 35-42 Post-hCG
Safety Issue?	No

Analysis Population Description

The modified ITT population. Number of participants analyzed (N) signifies those participants who were evaluated for this outcome measure.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	39	36
Number of Participants With Multiple Pregnancies [units: participants]	6	9

10. Secondary Outcome Measure:

Measure Title	Serum Progesterone (P4) Levels
Measure Description	
Time Frame	End of stimulation cycle (approximately 28 days)
Safety Issue?	No

Analysis Population Description

The modified ITT population included all participants randomized into trial who received at least 1 dose of GONAL-f®, and who completed primary efficacy assessment (total number of oocytes retrieved per participant following GONAL-f® stimulation and hCG injection). Participants were analyzed based on treatment they received.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	86	93
Serum Progesterone (P4) Levels [units: nmol/L] Mean (Standard Deviation)	5.41 (7.57)	4.88 (2.22)

Statistical Analysis 1 for Serum Progesterone (P4) Levels

Statistical Analysis Overview	Comparison Groups	GONAL-f ® CONSORT Calculator, GONAL-f ® Standard Treatment
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.235
	Comments	[Not specified]
	Method	ANOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	0.93
	Confidence Interval	(2-Sided) 95% -0.61 to 2.47
	Parameter Dispersion	Type: Standard Error of the mean Value: 0.78
	Estimation Comments	[Not specified]

11. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Clinical Pregnancy
Measure Description	Clinical pregnancy is defined by the number of sacs and hearts with activity per ultrasound scan performed on Day 35-42 post-hCG.
Time Frame	Day 35-42 Post-hCG
Safety Issue?	No

Analysis Population Description

The modified ITT population included all participants randomized into trial who received at least 1 dose of GONAL-f®, and who completed primary efficacy assessment (total number of oocytes retrieved per participant following GONAL-f® stimulation and hCG injection). Participants were analyzed based on treatment they received.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	86	93
Percentage of Participants With Clinical Pregnancy [units: percentage of participants]	36.0	35.5

Statistical Analysis 1 for Percentage of Participants With Clinical Pregnancy

Statistical Analysis Overview	Comparison Groups	GONAL-f ® CONSORT Calculator, GONAL-f ® Standard Treatment
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Percent difference]
	Estimated Value	0.6
	Confidence Interval	(2-Sided) 95% -13.5 to 14.6
	Estimation Comments	[Not specified]

12. Secondary Outcome Measure:

Measure Title	Number of Participants With OHSS
Measure Description	OHSS is a syndrome which can manifest with enlarged ovaries, advanced ascites with increased vascular permeability, pleural fluid accumulation, hemoconcentration, and increased blood clotting.
Time Frame	Start of treatment until Day 15-20 Post-hCG
Safety Issue?	Yes

Analysis Population Description

Safety population included all the participants who were randomized.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	96	104
Number of Participants With OHSS [units: participants]	6	13

13. Secondary Outcome Measure:

Measure Title	Pregnancy Outcome - Number of Participants With Pregnancy and Their Outcome
Measure Description	Pregnancy outcomes are live outcome (live infant) and non-live outcome (non-live infant) or unknown outcome (subject lost to follow-up).
Time Frame	up to 9 month (following the end of treatment)
Safety Issue?	No

Analysis Population Description

The modified ITT population included all participants randomized into trial who received at least 1 dose of GONAL-f®, and who completed primary efficacy assessment (total number of oocytes retrieved per participant following GONAL-f® stimulation and hCG injection). Participants were analyzed based on treatment they received.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.

	Description
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant's ovarian response and according to the center's standard practice.

Measured Values

	GONAL-f ® CONSORT Calculator	GONAL-f ® Standard Treatment
Number of Participants Analyzed	31	33
Pregnancy Outcome - Number of Participants With Pregnancy and Their Outcome [units: participants]		
Live outcomes	24	25
Non-live outcomes	2	3
Unknown outcomes	5	5

Reported Adverse Events

Time Frame	Adverse Events (AEs) were collected on an ongoing basis from day of written informed consent. All new AEs must be recorded until the final treatment examination, on Day 15-20 of the post-treatment assessment period
Additional Description	Pre-Treatment:Medical conditions present at the initial study visit that did not worsen in severity or frequency during the study; Treatment-Emergent: If the onset date of the AE was on or after the first dose date of the study medication.

Reporting Groups

	Description
GONAL-f ® CONSORT Calculator	GONAL-f® (follitropin alfa) administered subcutaneously (sc), dose ranging from 112.5 to 450 International Unit (IU) per day based on participant baseline characteristics determined according to the consistency in recombinant follicle stimulating hormone [r-FSH] starting doses for individualized treatment (CONSORT) calculator throughout stimulation cycle.
GONAL-f ® Standard Treatment	GONAL-f® (follitropin alfa) administered sc at a standard dose of 150 IU per day up to Day 5 of stimulation (S5) after which the dose was adjusted based upon the participant’s ovarian response and according to the center’s standard practice.

Serious Adverse Events

	GONAL-f ® CONSORT Calculator		GONAL-f ® Standard Treatment	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	4/96 (4.17%)		3/104 (2.88%)	
Musculoskeletal and connective tissue disorders				
Intervertebral disc protrusion [A] *	1/96 (1.04%)	1	0/104 (0%)	0
Pregnancy, puerperium and perinatal conditions				
Ectopic pregnancy [A] *	1/96 (1.04%)	1	0/104 (0%)	0
Reproductive system and breast disorders				
Ovarian hyperstimulation syndrome [A] *	2/96 (2.08%)	2	2/104 (1.92%)	2
Skin and subcutaneous tissue disorders				
Urticaria [A] *	0/96 (0%)	0	1/104 (0.96%)	1

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (Unspecified)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	GONAL-f ® CONSORT Calculator		GONAL-f ® Standard Treatment	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	40/96 (41.67%)		48/104 (46.15%)	
Gastrointestinal disorders				
Abdominal distension [A] *	8/96 (8.33%)	8	3/104 (2.88%)	5
Nausea [A] *	8/96 (8.33%)	9	9/104 (8.65%)	11
Injury, poisoning and procedural complications				
Procedural pain [A] *	9/96 (9.38%)	9	5/104 (4.81%)	5
Nervous system disorders				
Headache [A] *	18/96 (18.75%)	30	25/104 (24.04%)	40
Reproductive system and breast disorders				

	GONAL-f ® CONSORT Calculator		GONAL-f ® Standard Treatment	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Adnexa uteri pain [A] *	9/96 (9.38%)	10	8/104 (7.69%)	9
Ovarian hyperstimulation syndrome [A] *	5/96 (5.21%)	5	11/104 (10.58%)	12

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (Unspecified)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The PI shall submit any results communication to the sponsor for review and comment at least 30 business days prior to submission. The sponsor shall have the right to request the PI to delete or modify any of sponsor’s proprietary information contained therein. If the PI does not agree to the deletion or appropriate modification of such information, it shall postpone submission for publication or presentation for 60 days from the date the PI notifies the sponsor.

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