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

ClinicalTrials.gov ID: NCT01185704

Study Identification

Unique Protocol ID:	EMR200088-501
Brief Title:	Analysis of Two Therapeutic With Cetrotide® in Polycystic Ovarian (PCO) Women in Assisted Reproductive Technology (ART) (ATTAC-PCO)
Official Title:	A Phase IIIb Randomized Open-label Study to Compare the Estradiol Level on the Releasing Day in Two Regimen of Cetrotide® 0.25 mg Used From Day 1 or From Day 7 of the Menstrual Cycle (Day 0 or Day 6 of Stimulation) in Polycystic Ovarian (PCO) Women in ART (IVF/ICSI).
Secondary IDs:	2007-007932-25 [EudraCT Number] INI 28091 [Merck KGaA]

Study Status

Record Verification:	January 2014
Overall Status:	Completed
Study Start:	November 2008
Primary Completion:	October 2011 [Actual]
Study Completion:	February 2012 [Actual]

Sponsor/Collaborators

Sponsor:	Merck KGaA
Responsible Party:	Sponsor
Collaborators:	Merck Serono S.A.S, France

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 2-08-06/Avis n°2 Board Name: COMITE de PROTECTION des PERSONNES SUDOUEST ET OUTRE MER II Board Affiliation: COMITE de PROTECTION des PERSONNES SUDOUEST ET OUTRE MER II Phone: +33561779764/+33561779765 Email: ccpsoom1-2@vhu-toulouse.fr
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)

Study Description

Brief Summary: This is a randomized open-label study to compare between in-vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) outcomes of the two regimen of Cetrotide® (Cetrorelix acetate) which are 0.25 milligram (mg) used from Day 1 or Day 7 of the menstrual cycle (Day 0 or Day 6 of stimulation) in polycystic ovarian (PCO) women in assisted reproductive technology (ART).

Detailed Description: Polycystic ovarian syndrome population is an androgenic syndrome characterized by a wide spectrum of clinical manifestations such as obesity, hirsutism, insulin resistance, diabetes and presence of specific ultrasonic features.

Cetrotide®, cetrorelix acetate, is an antagonist of luteinizing-hormone-releasing hormone (LHRH). Cetrotide® is registered in 70 countries (including France) for the prevention of premature ovulation in subjects undergoing a controlled ovarian stimulation, followed by oocyte pick-up and ARTs. Ovitrelle®, active ingredient human chorionic-gonadotropin alfa, is administered to trigger final follicular maturation and luteinization after stimulation of follicular growth.

OBJECTIVES

Primary objective:

- To compare the hormonal level of plasmatic estradiol on the releasing day (day of r-hCG administration) induced by Cetrotide® 0.25 mg/day started on Day 1 (Group A: Day 1) or on Day 7 (Group B: Day 7) of the menstrual cycle (Day 0 (S0) or Day 6 (S6) of stimulation) in PCO subjects undergoing IVF/ICSI procedures.

Secondary objectives:

- To compare the hormonal changes during the stimulation induced by Cetrotide® in A and B Groups
- To assess by ultrasound scans (US) the follicular development induced by Cetrotide® in A and B Groups
- To assess biological and clinical outcomes induced by Cetrotide® in A and B Groups
- To monitor safety of Cetrotide in A and B Groups

The trial will be conducted on an outpatient basis. Once each subject has met all eligibility criteria, they will be randomly assigned in one of the two treatment groups.

Conditions

Conditions: Polycystic Ovarian Syndrome

Keywords: Cetrorelix acetate; follitropin alfa; human chorionic-gonadotropin alfa; follicular maturation; pregnancy; ovarian stimulation

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 3

Intervention Model: Parallel Assignment

Number of Arms: 2

Masking: Open Label

Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 136 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Day 1 protocol	Drug: Cetrorelix acetate Cetrotide® 0.25 mg will be administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) until r-hCG day (at least 2 follicles >=17 mm) Other Names: • Cetrotide® Drug: Recombinant Human Choriogonadotropin (r-hCG) The r-hCG will be administered subcutaneously as a single dose of 250 microgram (mcg) on r-hCG day Other Names: • Ovitrelle® Drug: Recombinant human follicle stimulating hormone (r-hFSH)

Arms	Assigned Interventions
	Recombinant human follicle stimulating hormone (r-hFSH) will be administered subcutaneously at a dose between 75 and 187.5 international unit (IU) once daily from Day 2 (Day 1 of stimulation period [S1]) until r-hCG day
Experimental: Day 7 protocol	Drug: Cetrorelix acetate Cetrotide® 0.25 mg will be administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) until r-hCG day (at least 2 follicles >=19 mm) Other Names: • Cetrotide® Drug: Recombinant Human Choriogonadotropin (r-hCG) The r-hCG will be administered subcutaneously as a single dose of 250 microgram (mcg) on r-hCG day Other Names: • Ovitrelle® Drug: Recombinant human follicle stimulating hormone (r-hFSH) Recombinant human follicle stimulating hormone (r-hFSH) will be administered subcutaneously at a dose between 75 and 187.5 international unit (IU) once daily from Day 2 (Day 1 of stimulation period [S1]) until r-hCG day

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 35 Years

Gender: Female

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Female subjects with PCO or Polycystic ovary syndrome (PCOS) according to the revised 2003 Rotterdam Consensus
- Female subjects suitable for IVF/ICSI, undergoing first or second attempt
- 18-35 years old, Body Mass Index (BMI) less than or equal to 32, non-smoking at least from Visit 0 (V0)
- Normal FSH value (less than 10 international unit per liter [IU/L]) on Day 3 of spontaneous cycle within 12 months prior to the trial

- Anti Mullerian Hormone (AMH) value (greater than 1.5 nanogram per milliliter [ng/mL]) of a spontaneous cycle within 12 months prior to the trial or at least at V0
- No history of active genito-urinary infection
- Normal thyroid function (or adequate substitution for at least 3 months)
- Negative cervical papanicolaou test within the last 12 months prior to study entry
- No gonadotropins, for at least one month prior to the trial
- No metformin therapy for at least one month prior to Visit 1 (V1)
- Subject who is able to participate in the trial and has provided written, informed consent.

Exclusion Criteria:

- Ongoing pregnancy, any pregnancy within 3 months prior to study entry, or any contraindication to pregnancy or carrying pregnancy to term
- Drilling 3 months prior to V0
- Uterine malformation, diethylstilbestrol syndrome, synechia
- Female subjects with World Health Organization (WHO) Type I or III anovulation
- Female subjects with hyperprolactinemia
- Female subjects with more than 2 recurrent miscarriages (early or late, and for any reasons)
- Known infection with Human Immunodeficiency Virus (HIV), Hepatitis B or C virus, for subject or partner
- Abnormal gynecological bleeding of undetermined origin
- History of major thromboembolic disease
- Endometriosis (Grade III or IV)
- Presence or history of malignant tumors and related treatment
- Known case of tumors of the hypothalamus or pituitary gland
- Clinically significant systemic disease or clinically significant abnormal hematology, chemistry, or urinalysis results at screening
- Known allergic reaction or hypersensitivity to Cetrotide® or Ovitrelle®
- Any active substance abuse or history of drug, medication or alcohol abuse in the past 5 years
- Participation in another clinical trial within 3 months prior to study entry.

Contacts/Locations

Study Officials: Dr Etienne VARLAN
Study Director
Merck Lipha Santé

Locations: France
Research Site
Toulouse, France

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Overall Study

	Day 1 Protocol	Day 7 Protocol
Started	68	68
Treated	65	65
Completed	55	60
Not Completed	13	8
Randomized but not treated	3	3
Lack of ovarian response	5	1
Ovarian hyperstimulation syndrome risk	5	3
Ectopic pregnancy	0	1

Baseline Characteristics

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Baseline Measures

	Day 1 Protocol	Day 7 Protocol	Total
Number of Participants	65	65	130
Age, Continuous [units: years] Mean (Standard Deviation)	29.7 (2.9)	29.7 (3.3)	29.7 (3.1)
Gender, Male/Female [units: participants]			
Female	65	65	130
Male	0	0	0

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Estradiol (E2) Levels on r-hCG Day
Measure Description	
Time Frame	r-hCG day (end of stimulation cycle [approximately 15 days])
Safety Issue?	No

Analysis Population Description

Intent to treat (ITT) population included all randomized participants who had received at least 1 dose of the study medication. N" (number of participants analyzed) signifies those participants who were evaluable for this measure.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	58	62
Estradiol (E2) Levels on r-hCG Day [units: picogram/milliliter (pg/mL)] Mean (Standard Deviation)	1668.86 (862.62)	1672.80 (835.49)

2. Secondary Outcome Measure:

Measure Title	Serum Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH) Levels
Measure Description	
Time Frame	Day 1
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication. N" (number of participants analyzed) signifies those participants who were evaluable for this measure. Here "n" signifies those participants who were evaluated for specified category.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

	Description
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	58	62
Serum Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH) Levels [units: International unit/liter (IU/L)] Mean (Standard Deviation)		
LH levels (n=58, 62)	4.87 (4.62)	6.84 (3.99)
FSH levels (n=57, 59)	4.98 (1.54)	6.69 (10.29)

3. Secondary Outcome Measure:

Measure Title	Serum Estradiol (E2) Levels
Measure Description	
Time Frame	Day 1
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication. 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

	Description
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	60	63
Serum Estradiol (E2) Levels [units: pg/mL] Mean (Standard Deviation)	30.42 (14.06)	68.79 (116.09)

4. Secondary Outcome Measure:

Measure Title	Serum Progesterone (P4) Levels
Measure Description	
Time Frame	Day 1
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication. 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	59	62
Serum Progesterone (P4) Levels [units: nanomolar/liter (nmol/L)] Mean (Standard Deviation)	0.83 (0.72)	0.97 (1.82)

5. Secondary Outcome Measure:

Measure Title	Anti Mullerian Hormone (AMH) Levels
Measure Description	
Time Frame	Day 0
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication. 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	63	64
Anti Mullerian Hormone (AMH) Levels [units: nanogram/milliliter (ng/mL)] Mean (Standard Deviation)	6.27 (4.40)	7.18 (4.11)

6. Secondary Outcome Measure:

Measure Title	Number of Follicles Greater Than or Equal (>=) to 17 mm (For Day 1 Protocol) or 19 mm (For Day 7 Protocol) on r-hCG Day
Measure Description	
Time Frame	r-hCG day (end of stimulation cycle [approximately 15 days])
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication. 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	58	61
Number of Follicles Greater Than or Equal (>=) to 17 mm (For Day 1 Protocol) or 19 mm (For Day 7 Protocol) on r-hCG Day [units: follicles] Mean (Standard Deviation)	3.55 (2.20)	2.49 (1.99)

7. Secondary Outcome Measure:

Measure Title	Number and Quality of Oocytes Retrieved

Measure Description	Oocyte retrieval is a technique used in in-vitro fertilization (IVF) in order to remove oocytes from the ovary of the female participant, enabling fertilization outside the body. Oocytes were classified into 4 different categories based on their quality: mature, fractured, immature and inseminated oocytes.
Time Frame	Oocytes retrieval day (36 +/- 2 hours post r-hCG day [end of stimulation cycle {approximately 15 days}])
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	65	65
Number and Quality of Oocytes Retrieved [units: oocytes] Mean (Standard Deviation)		
Total number of oocytes	7.48 (5.21)	8.11 (5.55)
Mature oocytes	2.52 (4.07)	3.72 (4.43)
Fractured oocytes	0.09 (0.34)	0.11 (0.44)
Immature oocytes	0.98 (2.29)	1.38 (2.55)
Inseminated oocytes	3.06 (4.14)	4.52 (4.66)

8. Secondary Outcome Measure:

Measure Title	Total Dose of Recombinant Human Follicle Stimulating Hormone (r-hFSH)
Measure Description	
Time Frame	Day 1 up to r-hCG day (end of stimulation cycle [approximately 15 days])
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication. 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	64	65
Total Dose of Recombinant Human Follicle Stimulating Hormone (r-hFSH) [units: international unit (IU)] Mean (Standard Deviation)	1462.50 (537.85)	1221.35 (478.31)

9. Secondary Outcome Measure:

Measure Title	Percentage of Fertilized Oocytes Retrieved
Measure Description	Oocytes were fertilized using Intra-cytoplasmic Sperm Injection (ICSI) technique which is an IVF procedure in which a single sperm is injected directly into an egg under a microscope.
Time Frame	Oocytes retrieval day (36 +/- 2 hours post r-hCG day [end of stimulation cycle {approximately 15 days}])

Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication. 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	56	61
Percentage of Fertilized Oocytes Retrieved [units: percent fertilized oocytes] Mean (Standard Deviation)	46.22 (30.66)	46.86 (30.54)

10. Secondary Outcome Measure:

Measure Title	Number of Embryos
Measure Description	Embryo is defined as the product of the zygote, two or three days after fertilization of the oocytes.
Time Frame	Day 2-3 post oocytes retrieval day (36 +/- 2 hours post r-hCG day [end of stimulation cycle {approximately 15 days}])
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	65	65
Number of Embryos [units: embryos] Mean (Standard Deviation)	3.18 (3.18)	3.60 (3.27)

11. Secondary Outcome Measure:

Measure Title	Number of Blastocysts
Measure Description	Blastocyst is an embryo, five or six days after fertilization, with an inner cell mass, outer layer of trophectoderm and a fluid-filled blastocoele cavity.
Time Frame	Day 5-6 post oocytes retrieval day (36 +/- 2 hours post r-hCG day [end of stimulation cycle {approximately 15 days}])
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

	Description
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	65	65
Number of Blastocysts [units: blastocysts] Mean (Standard Deviation)	0.26 (1.05)	0.20 (0.90)

12. Secondary Outcome Measure:

Measure Title	Number of Transferred Embryos
Measure Description	Embryo transfer is the procedure in which one or more embryos are placed in the uterus.
Time Frame	Day 2-3 post Oocytes retrieval day (36 +/- 2 hours post r-hCG day [end of stimulation cycle {approximately 15 days}])
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	65	65
Number of Transferred Embryos [units: transferred embryos] Mean (Standard Deviation)	0.95 (0.74)	1.02 (0.74)

13. Secondary Outcome Measure:

Measure Title	Implantation Rate
Measure Description	Implantation rate per reporting group was measured as the number of gestational sacs observed, divided by the number of embryos transferred multiplied by 100.
Time Frame	5 weeks post oocytes retrieval day (36 +/- 2 hours post r-hCG day [end of stimulation cycle {approximately 15 days}])
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication. 'N' (number of participants analyzed) signifies those participants who were evaluable for this measure.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	46	48
Implantation Rate [units: percent sacs per embryo]	36.90	32.25

14. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Clinical Pregnancy
Measure Description	Clinical pregnancy was defined as pregnancy diagnosed by ultrasonographic visualization of one or more gestational sacs or definitive clinical signs of pregnancy. It excludes ectopic pregnancy.
Time Frame	10 weeks post r-hCG day (end of stimulation cycle [approximately 15 days])
Safety Issue?	No

Analysis Population Description

ITT population included all randomized participants who had received at least 1 dose of the study medication.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	65	65
Percentage of Participants With Clinical Pregnancy [units: percentage of participants]	20	20

15. Secondary Outcome Measure:

Measure Title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

Measure Description	An adverse event (AE) was defined as any untoward medical occurrence in the form of signs, symptoms, abnormal laboratory findings, or diseases that emerges or worsens relative to baseline during a clinical study with an Investigational Medicinal Product (IMP), regardless of causal relationship and even if no IMP has been administered. A Serious Adverse Event (SAE) was an AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial or prolonged inpatient hospitalization; congenital anomaly/birth defect. To avoid the participant/event combination double-count AEs and SAEs are reported separately.
Time Frame	Day 1 up to end of study (15 days post last administration of study drug)
Safety Issue?	Yes

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Measured Values

	Day 1 Protocol	Day 7 Protocol
Number of Participants Analyzed	65	65
Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs) [units: participants]		
AEs	11	18
SAEs	2	4

Reported Adverse Events

Time Frame	Day 1 up to end of study (15 days post last administration of study drug)
Additional Description	An adverse event (AE) was defined as any untoward medical occurrence in the form of signs, symptoms, abnormal laboratory findings, or diseases that emerges or worsens relative to baseline during a clinical study with an Investigational Medicinal Product (IMP), regardless of causal relationship and even if no IMP has been administered.

Reporting Groups

	Description
Day 1 Protocol	Cetrotide® 0.25 milligram (mg) was administered subcutaneously once daily from Day 1 (Day 0 of stimulation period [S0]) along with Recombinant human follicle stimulating hormone (r-hFSH) at a dose between 75 and 187.5 international unit (IU) subcutaneously once daily from Day 2 (Day 1 of stimulation period [S1]) until recombinant human chorionic gonadotropin (r-hCG) administration day (at least 2 follicles greater than or equal to (>=) 17 millimeter [mm]). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.
Day 7 Protocol	Cetrotide® 0.25 mg was administered subcutaneously once daily from Day 7 (Day 6 of stimulation period [S6]) along with r-hFSH at a dose between 75 and 187.5 IU subcutaneously once daily from Day 2 (S1) until r-hCG administration day (at least 2 follicles >= 19 mm). On r-hCG day, 250 microgram of r-hCG was administered once subcutaneously.

Serious Adverse Events

	Day 1 Protocol	Day 7 Protocol
	Affected/At Risk (%)	Affected/At Risk (%)
Total	2/65 (3.08%)	4/65 (6.15%)
Pregnancy, puerperium and perinatal conditions		
Ectopic pregnancy [A] *	0/65 (0%)	1/65 (1.54%)
Reproductive system and breast disorders		
Ovarian Hyperstimulation syndrome [A] *	2/65 (3.08%)	3/65 (4.62%)

* 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: 0%

	Day 1 Protocol	Day 7 Protocol
	Affected/At Risk (%)	Affected/At Risk (%)
Total	9/65 (13.85%)	14/65 (21.54%)
Gastrointestinal disorders		
Abdominal pain [A] *	0/65 (0%)	1/65 (1.54%)
Anal fissure [A] *	1/65 (1.54%)	0/65 (0%)
Nausea [A] *	2/65 (3.08%)	1/65 (1.54%)
General disorders		
Injection site burning [A] *	1/65 (1.54%)	0/65 (0%)
Injection site erythema [A] *	1/65 (1.54%)	1/65 (1.54%)
Injection site irritation [A] *	1/65 (1.54%)	0/65 (0%)
Injection site pain [A] *	0/65 (0%)	1/65 (1.54%)
Injection site pruritus [A] *	1/65 (1.54%)	1/65 (1.54%)
Pyrexia [A] *	1/65 (1.54%)	0/65 (0%)
Investigations		
Oestradiol increased [A] *	1/65 (1.54%)	0/65 (0%)
Nervous system disorders		
Headache [A] *	6/65 (9.23%)	1/65 (1.54%)
Reproductive system and breast disorders		
Adnexa uterin pain [A] *	1/65 (1.54%)	0/65 (0%)
Metrorrhagia [A] *	0/65 (0%)	1/65 (1.54%)
Ovarian Hyperstimulation syndrome [A] *	0/65 (0%)	6/65 (9.23%)
Pelvic pain [A] *	4/65 (6.15%)	3/65 (4.62%)
Vascular disorders		

	Day 1 Protocol	Day 7 Protocol
	Affected/At Risk (%)	Affected/At Risk (%)
Hot flush [A] *	1/65 (1.54%)	0/65 (0%)

* 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.

Results Point of Contact:

Name/Official Title: Merck KGaA Communication Center
Organization: Merck Serono, a division of Merck KGaA
Phone: +49-6151-72-5200
Email: service@merckgroup.com