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Different routes of progesterone administration for sustaining implantation in in vitro fertilisation patients: impact on pregnancy and live birth rates

Submission date
02/08/2023

Recruitment status
No longer recruiting

Registration date
15/08/2023

Overall study status
Completed

Last Edited
27/12/2024

Condition category
Pregnancy and Childbirth

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Progesterone administration is considered an essential therapy for luteal phase support in patients undergoing in-vitro fertilization (IVF) technologies This study aims to compare the administration of a combined protocol of vaginal gel progesterone (90 mg/daily) and oral dydrogesterone (20 mg/daily), with the administration of micronized vaginal progesterone alone (800 mg daily) to support the luteal phase during embryo implantation in patients undergoing in vitro fertilization.

Who can participate
Infertile patients undergoing standard in-vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) treatment at One Day Medical Center IVF Unit

What does the study involve
Ovarian stimulation:
All the patients will undergo a mild ovarian stimulation protocol:
Subcutaneous injections of recombinant follicle-stimulating hormone (rFSH) will be started at a dose of 75-150 IU (international unit). Growing ovarian follicles will be detected and measured using ultrasonography at two-day intervals. Estradiol blood level will be measured at two days intervals. Subcutaneous injections of Gonadotropin-releasing hormone antagonist (GnRH ant) (0.25 mg/day) will be administered when the leading follicle measures 14 mm. The rFSH dose will be adjusted when necessary according to the follicular size and estradiol level. Final oocyte maturation will be induced by subcutaneous injection of a dose of 10,000 IU of Human Chorionic Gonadotropin (hCG).

Oocyte recovery and embryo transfer
Oocyte retrieval will be carried out at 34-36 hours after hCG injection. Recovered oocytes will be inseminated by standard IVF or ICSI. Up to 3 embryos will be transferred into the patient's uterus on day three after the oocyte insemination.

What are the possible benefits and risks of participating?
Benefits: the applied supplementation therapy for luteal phase support after embryo replacement could increase the pregnancy and live birth rates.
Risks: the applied supplementation therapy for luteal phase support after embryo replacement could reduce the chance of pregnancy and live birth.

Where is the study run from?
One Day Medical Center s.r.l. (Italy)

When is the study starting and how long is it expected to run for?
October 2016 to December 2022

Who Is funding the study?
One Day Medical Center s.r.l. (Italy)

Who is the main contact?
Leonardo Rinaldi, Leo.rinaldi@tiscali.it

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
oneday20161

Study information

Scientific Title

Oral dydrogesterone associated with vaginal micronized progesterone supplementation vs vaginal micronized progesterone alone supplementation for luteal phase support in in vitro fertilization patients: effects on pregnancy and live birth rates

Study objectives
To compare the administration of a combined protocol of progesterone vaginal gel and oral dydrogesterone, with the administration of micronized vaginal progesterone alone for luteal phase support in patients undergoing GnRH antagonist-mild stimulation regimen

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 10/12/2016, One Day Ethics Commission (Via Attilio Ambrosini 114, Roma, 00147, Italy; +39 (0)645212028; amministrazione@onedaymedicalcenter.it), ref: ethics12-2016

Study design
Prospective open randomized study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Medical and other records

Study type(s)
Treatment, Efficacy

Participant information sheet
Not applicable

Health condition(s) or problem(s) studied
Luteal phase supplementation in assisted reproduction

Interventions
All the patients are going to have a mild ovarian stimulation protocol:
rFSH will be started at a dose of 75-150 IU on the base of AMH level. GnRH antagonist (0.25 mg /day) will be administered when the leading follicle measures 14 mm. The FSH dose will be adjusted when necessary according to the follicular size and estradiol level. Final oocyte maturation will be induced by a dose of 10,000 IU of hCG. Recovered oocytes will be inseminated by standard IVF or intracytoplasmic sperm injection (ICSI). Up to three embryos will be transferred on day 3 after oocyte insemination.

Randomization will be performed using a computer-generated random assignment schedule for each patient. Sealed and numbered envelopes will be used to conceal the treatment allocation until randomization. On the day of oocyte recovery, the patients will be randomized into two groups: Group A will receive vaginal administration of capsules of micronized progesterone (800 mg/day) for luteal phase support; Group B will receive a combination of vaginal administration

of a gel of micronized progesterone (90 mg/day) and oral dydrogesterone 10 mg twice a day for luteal phase support. The duration of the treatment is 14 - 21 days; follow-up will be around 9 months for each patient, from the established pregnancy to the delivery.

Intervention Type
Drug

Pharmaceutical study type(s)
Dose response

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Oral dydrogesterone, micronized vaginal progesterone

Primary outcome measure
Clinical pregnancy measured using a blood test to evaluate the level of human chorionic gonadotropin (hCG), which indicates the eventual embryo implantation and pregnancy, 14 days after embryo replacement in the patient's uterus

Secondary outcome measures
Embryo implantation rate measured using ultrasonography at 4 weeks following a positive hCG test to confirm the clinical pregnancy

Overall study start date
15/10/2016

Completion date
23/12/2022

Eligibility

Key inclusion criteria
1. Infertility attributable to tubal factors, moderate endometriosis, male factor, or idiopathic infertility
2. Serum hormonal profile within the normal range (AMH >1 ng/ml)
3. Regular menstrual cycles
4. The presence of a normal uterine cavity
5. Body mass index (BMI) of 20–26 kg/m²

Participant type(s)
Patient

Age group
Adult

Lower age limit
27 Years

Upper age limit
41 Years

Sex
Female

Target number of participants
650

Total final enrolment
620

Key exclusion criteria
1. Infertility attributable to genetic factors or severely reduced ovarian reserve
2. Serum hormonal profile showing a reduced ovarian reserve (AMH <0.9 ng/ml)
3. Irregular menstrual cycles or amenorrhea
4. Congenital or acquired uterine malformation
5. A body mass index (BMI) <20 or >26 kg/m²

Date of first enrolment
01/01/2017

Date of final enrolment
01/11/2022

Locations

Countries of recruitment
Italy

Study participating centre
One Day Medical Center - PMA Unit
Via Attilio Ambrosini 114
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Sponsor information

Organisation
One Day Medical Center srl

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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
One Day Medical Center s.r.l

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/12/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made avalilable due to lack of consensus

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		21/12/2024	27/12/2024	Yes	No