At-Home IVF Kit: application during the COVID-19 pandemic

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Summary
The guidelines, at the time of writing this manuscript, recommend withholding fertility treatments due to fear of the COVID-19. However, many fertility doctors and many patients, especially those with diminished ovarian reserve (DOR), strongly suggest that their fertility treatment including oocyte and/or embryo freezing is a time-sensitive matter due to fear of losing all their ovarian reserve. This report presents a novel approach for ovarian stimulation at home in women with DOR for oocyte/embryo cryopreservation using At-HOME IVF kit mailed to the patients’ home, and without the need for blood hormones and transvaginal ultrasounds monitoring. In this study, women (n = 22) diagnosed with DOR who underwent either oocyte (n = 6) or embryo freezing (n = 16) were included. Each patient took the medications included in the kit without the frequent visits to the office for monitoring and presented only once to the fertility clinic on the day of the oocyte retrieval. Upon presentation on the day of oocyte retrieval, none of the patients had ovulated. All patients underwent oocyte retrieval with 21 out of 22 patients having had at least one or more oocytes collected, with the number of mature oocytes retrieved ranging from 1 to 7. Eight out of 16 patients (50%) who underwent IVF, had embryos cryopreserved at either the cleavage-stage or blastocyst stage. This report suggests that, during the COVID-19 pandemic, At-HOME IVF kit presents a novel solution for women with DOR, or in situations where time is of essence, limiting office visits and thus minimizing the risk of coronavirus infection.

Key words: IVF; Home; Coronavirus; COVID-19; Oocyte freezing; Pandemic.

Introduction
The coronavirus disease 2019 (COVID-19), also called the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), is rapidly spreading all over the world causing a serious global public health issue [1]. During this pandemic, access to fertility has been difficult due to fear of transmission of the virus from patient to patient or from patient to clinic staff members (or vice versa).

On March 17, 2020, the American Society for Reproductive Medicine (ASRM) released new clinical recommendations [2] stating that clinics: 1) do not initiate new treatment cycles — including ovulation induction, intrauterine insemination (IUI), in-vitro fertilization (IVF) (both oocyte retrievals and frozen embryo transfers), and non-urgent oocyte or embryo freezing, 2) strongly consider canceling all embryo transfers (fresh or frozen), 3) continue caring for people who are “in-cycle,” or have urgent needs for stimulation or cryopreservation (oocyte or embryo freezing), 4) postpone elective surgeries and any non-urgent diagnostic procedures, and 5) prioritize telehealth over in-person contact. Additionally, the society for assisted reproductive technology (SART) recommended that anyone who is actively pursuing assisted reproductive technology (ART) and meets the diagnostic criteria for the COVID-19 infection consider freezing all oocytes or embryos and waiting until patients are disease-free to do an embryo transfer [3].

On March 19, 2020, the European Society of Human Reproduction and Embryology (ESHRE) recommended a precautionary approach and advised all infertility patients considering or planning treatment to avoid becoming pregnant at this time and they further suggested consideration of deferred pregnancy with oocyte or embryo cryopreservation [4]. Despite these recommendations and other experts’ commentaries [5, 6], many fertility doctors and many patients (especially those older than 38 years old and those with diminished ovarian reserve [DOR]) strongly believe and expressed that their fertility treatment (i.e., oocyte and/or embryo freezing) is time-sensitive, even though it is not considered urgent care.

Given this challenging situation and in order to minimize the repeated office visits for monitoring during an IVF cycle, we aimed to test a new modality for IVF treatment using a kit called At-HOME IVF kit. This kit that contains all the necessary medications (oral pills, vaginal pills, and nasal spray) needed for ovarian stimulation, ovulation suppression, and oocyte maturation trigger. During the treatment cycle using the kit, patients did not do any monitoring for frequent blood hormone levels or any transvaginal ultrasound for follicular measurement. Each patient needed to go to the office only once on the day of the oocyte retrieval procedure.

Methods
This is a retrospective case series study that assessed the response and outcome using the At-HOME IVF kit in
Table 1. — Description of the dose and mode of administration of the medications used in the HOME IVF kit based on the day of the menstrual cycle of the patient.

| CYCLE DAY | ORAL MEDICATIONS | NASAL SPRAY | VAGINAL SUPPOSITORIES | URINE OVULATION TEST |
|-----------|-------------------|-------------|-----------------------|---------------------|
| 3         | 2 Clomiphene citrate tablets | 2 Letrozole tablets |                   |                     |
| 4         | 2 Clomiphene citrate tablets | 2 Letrozole tablets |                   |                     |
| 5         | 2 Clomiphene citrate tablets | 2 Letrozole tablets |                   |                     |
| 6         | 2 Clomiphene citrate tablets | 2 Letrozole tablets |                   |                     |
| 7         | 2 Clomiphene citrate tablets | 2 Letrozole tablets |                   |                     |
| 8         | 2 Clomiphene citrate tablets |                   |                     |                     |
| 9         | 2 Clomiphene citrate tablets | 1/4 of Elagolix tablet |                   |                     |
| 10        | 2 Clomiphene citrate tablets |                   |                     |                     |
| 11        | 2 Clomiphene citrate tablets | 1/4 Elagolix tablet |                     |                     |
| 12        | Leuprorelin (see Table 3 for details of use) | Urine test (AM and PM)* | Urine test (AM and PM)* |                     |
| 13        | Leuprorelin (see Table 3 for details of use) | Urine test (AM and PM)* | Urine test (AM and PM)* |                     |

* The result of the urine ovulation test (ovulation predictor kit) should be “negative” on day 11 of the menstrual cycle but “positive” after administration of the Leuprorelin nasal spray.

Table 2. — Instructions on the use of the nasal spray trigger for oocyte maturation in the evening of cycle day 12 of the menstrual cycle.

| LEUPRORELIN NASAL SPRAY INSTRUCTIONS |
|--------------------------------------|
| STEP 1 | Administer 3 puffs per nostril |
| STEP 2 | Wait 10 minutes |
| STEP 3 | Administer 3 puffs per nostril |

patients who have DOR (n = 22) based on previous history of poor ovarian response either at our center or at another fertility center, previously documented low serum anti-Mullerian hormone (AMH; < 1 ng/mL), previously documented elevated day 3 follicle-stimulating hormone (FSH; > 10 mIU/mL), or previously documented low antral follicle count by transvaginal ultrasound (AFC; < 8). Telemedicine was used for consultation, instead of an in-office visit, in order to reduce the total waiting time for seeking fertility treatment and in order to minimize exposure of patients to potentially infected individuals [7]. Each patient had a video details call with the physician in order to discuss her medical history, gynecologic/obstetric history, previous surgical history, medication intake, allergies, previous fertility treatment history, allergies, and social history. Exclusion criteria included irregular menstrual cycle or history of any medical conditions that prevent the intake of fertility drugs included in the kit. All patients underwent their fertility treatments at New Hope Fertility Center, New York from September 2019 until April 2020. The main outcome included the number of oocytes and embryos (cleavage-stage or blastocyst-stage depending on the patient’s preference) cryopreserved. Because of the COVID-19 pandemic, embryo transfer was not currently recommended. Approval for the study was obtained from New England Institutional Review Board (NEIRB# 16-130). All
patients used the At-HOME IVF kit and did not do any monitoring for blood hormone levels or transvaginal ultrasounds for follicular measurement until the day of the oocyte retrieval.

**Description of the At-HOME IVF kit**

Table 1 describes the medications included in the kit and displays an exemplary medication schedule for at-home controlled ovarian stimulation method. The physician discussed (over the phone or over a video call) all the medication schedule included in the kit and then mailed the kit comprising all the needed medications to the patient’s home.

Upon receiving the kit, on the start date (day 3 of the menstrual cycle), the patient was directed to orally take 100 mg of clomiphene citrate (Clomid®) and 5 mg of letrozole (Femara®), instead of the conventional daily injectable gonadotropins. The patient was then directed to take the same oral dosages of clomiphene citrate and letrozole daily on each of days 4-7 of the menstrual cycle. On day 8 of the menstrual cycle, the patient was directed to orally take only 100 mg of clomiphene citrate, and to stop the letrozole.

On day 9 of the menstrual cycle, the patient was directed to orally take 100 mg of clomiphene citrate and to insert vaginally the gonadotropin-releasing hormone (GnRH) antagonist elagolix (ORILISSA®). Elagolix has been used for treatment of endometriosis symptoms [8, 9] and recently used to suppress ovulation [10, 11], instead of the injectable ganirelix acetate (GANIRELEX®) or cetorelix acetate (CETROTIDE®) used routinely in conventional practices. A dose of 50 mg (1/4th of a 200 mg pill) of Elagolix was used. On day 10 of the menstrual cycle, the patient was directed to orally take only 100 mg of clomiphene citrate.

On day 11 of the cycle, the patient was directed to orally take 100 mg of clomiphene citrate and to insert vaginally Elagolix tablet (50 mg) as a suppository. Also, on day 11, the patient was directed to take a home urine ovulation test (included in the kit) in the morning (9 am) and in the evening (9 pm) to ensure that there was no signs of early ovulation. The results of the urine ovulation tests on day 11 should both be negative. A negative urine ovulation test indicates that Elagolix was properly suppressing the luteinizing hormone (LH) surge from occurring. However, if the results of either ovulation test on day 11 was positive, indicating the patient is having an LH surge, then the patient was advised to contact the physician in order to schedule the oocyte retrieval on the following day.

On days 12 of the menstrual cycle, the patient was directed to take doses of leuprolrelin (LUPRON®) dissolved in saline water as a nasal spray (1: 20 to 1: 40 dilution in saline, which is a total of 30 Units) prepared by a licensed pharmacist [12]. Leuprolrelin is available as a leuprolide acetate injection bottle containing 14 mg/2.8 mL. A 0.3 mL (30 Units) of the leuprolide acetate is added to 5.7 mL of sterile saline to a sterile nasal spray pump device to produce a 6 mL solution that produces 120 sprays. Thus, each spray contain 0.05 mL (6 mL/120 puffs) or 0.25 Units of leuprolide acetate. Conventionally, leuprolrelin is administered as an injection to the muscle or under the skin of the patient. However, in the kit, leuprolrelin was taken nasally by the patient [12]. Table 2 shows the details on the nasal spray use: 3 puffs (first step) of the nasal spray are self-administered by the patient per nostril, after 10 minutes of waiting (second step), the patient then self-administers 3 more puffs of the nasal spray per nostril (third step). Twelve hours later, the patient repeats steps 1 to 3.

On day 12 of the menstrual cycle, the patient was again

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**Table 3. — Serum LH hormone level before and after the intake of the conventional Ganirelex/Cetrotide injectable medication versus the vaginal elagolix pi.**

|                      | Serum LH level (mIU/mL) BEFORE medication intake | Serum LH level (mIU/mL) AFTER medication intake | % Drop in blood LH hormone level |
|----------------------|-----------------------------------------------|-----------------------------------------------|-------------------------------|
| **Conventional Ganirelex/Cetrotide injectables** |                                               |                                               |                               |
| Patient 1            | 4.3                                           | 2                                             | 53.5%                         |
| Patient 2            | 12.0                                          | 6.3                                           | 47.5%                         |
| Patient 3            | 12.0                                          | 4.9                                           | 59.2%                         |
| Patient 4            | 18.0                                          | 16                                            | 11.1%                         |
| Patient 5            | 14.6                                          | 14.1                                          | 3.4%                          |
| **Vaginal Elagolix pill** |                                               |                                               |                               |
| Patient 1            | 7.0                                           | 1.0                                           | 85.7%                         |
| Patient 2            | 16.7                                          | 5.7                                           | 65.9%                         |
| Patient 3            | 10.2                                          | 3.2                                           | 68.6%                         |
| Patient 4            | 8.2                                           | 1.7                                           | 79.3%                         |
| Patient 5            | 7.0                                           | 0.8                                           | 88.6%                         |
| Patient number | Age | Treatment cycle | Number of large follicles (between 14-22 mm on the day of oocyte retrieval) | Number of total oocytes retrieved (GV, MI, and MII) | Number of immature oocytes (GV or MI) retrieved | Oocytes/embryos cryopreserved |
|---------------|-----|-----------------|--------------------------------------------------------------------------|------------------------------------------------|---------------------------------------------|----------------------------------|
| 1             | 43  | Embryo freezing | 8                                                                        | 7                                                 | 1                                            | 2 blastocysts                    |
| 2             | 34  | Embryo freezing | 4                                                                        | 2                                                 | 0                                            | 1 blastocyst                     |
| 3             | 44  | Oocyte freezing | 2                                                                        | 1                                                 | 0                                            | 1 oocyte                         |
| 4             | 34  | Embryo freezing | 4                                                                        | 4                                                 | 2                                            | no blastocyst formed             |
| 5             | 41  | Oocyte freezing | 4                                                                        | 2                                                 | 0                                            | 2 oocytes                        |
| 6             | 30  | Embryo freezing | 1                                                                        | 1                                                 | 0                                            | no blastocyst formed             |
| 7             | 43  | Embryo freezing | 1                                                                        | 1                                                 | 0                                            | no blastocyst formed             |
| 8             | 41  | Embryo freezing | 2                                                                        | 1                                                 | 0                                            | no blastocyst formed             |
| 9             | 43  | Embryo freezing | 4                                                                        | 4                                                 | 0                                            | 1 cleavage-stage embryo          |
| 10            | 34  | Embryo freezing | 4                                                                        | 4                                                 | 1                                            | 1 blastocyst                     |
| 11            | 43  | Oocyte freezing | 5                                                                        | 2                                                 | 1                                            | 1 oocyte                         |
| 12            | 38  | Embryo freezing | 3                                                                        | 3                                                 | 0                                            | 2 cleavage-stage embryos         |
| 13            | 46  | Embryo freezing | 3                                                                        | 3                                                 | 0                                            | no blastocyst formed             |
| 14            | 38  | Embryo freezing | 3                                                                        | 3                                                 | 0                                            | 1 blastocyst                     |
| 15            | 41  | Embryo freezing | 2                                                                        | 2                                                 | 1                                            | no blastocyst formed             |
| 16            | 45  | Embryo freezing | 2                                                                        | 1                                                 | 0                                            | no blastocyst formed             |
| 17            | 44  | Oocyte freezing | 1                                                                        | 0                                                 | 0                                            | none                            |
| 18            | 37  | Embryo freezing | 3                                                                        | 1                                                 | 0                                            | 1 blastocyst                     |
| 19            | 43  | Embryo freezing | 5                                                                        | 4                                                 | 0                                            | 2 cleavage-stage embryos         |
| 20            | 36  | Embryo freezing | 5                                                                        | 1                                                 | 0                                            | Oocyte discarded due to poor quality |
| 21            | 42  | Oocyte freezing | 2                                                                        | 1                                                 | 0                                            | 1 oocyte                         |
| 22            | 38  | Oocyte freezing | 4                                                                        | 4                                                 | 0                                            | 4 oocytes                        |

directed to take a home urine ovulation test in the morning (9:00 am) and in the evening (9:00 pm). Both urine ovulation tests should be done before the nasal spray intake and both ovulation test results should be negative (for
the same reason as mentioned earlier on cycle day 11 of the menstrual cycle). The self-administration of the leuprorelin nasal spray should be done after 9:00 pm on that day.

On day 13 of the menstrual cycle, the patient is directed to take again a home urine ovulation test in the morning (9:00 am) and in the evening (9:00 pm). The results of the ovulation tests for the patient should be positive for both ovulation tests, indicating proper intake of the nasal spray as reflected usually by an LH surge, which is responsible for turning the urine ovulation test positive. If ovulation is not confirmed on day 13 (i.e., results of ovulation tests on day 13 are negative, which are most likely due to improper intake of the nasal spray), then the patient needs to contact the physician immediately, who will ask the patient to re-take properly the nasal spray. If ovulation is confirmed on day 13 (i.e., results of the ovulation tests are positive), then on day 14 the patient presents to the clinic for the oocyte retrieval procedure.

**Elagolix for prevention of ovulation**

By blocking the GnRH receptor, Elagolix suppresses LH release by the pituitary gland and thus prevents LH surge [10, 11]. Elagolix is generally an oral medication (oral tablet), however in the present kit, it is taken mainly as a vaginal suppository but may be taken orally based on the patient’s preference. In order to compare the efficacy of Elagolix on LH suppression, we compared the LH in 5 patients before (cycle day 9 on average) and after (cycle day 10 on average) the intake of Elagolix and in 5 women before and after the intake of the injectable ganirolex acetate (GANIRELEX®) or cetrotrex acetate (CETROTIDE®).

**Results**

Table 3 provides a comparison of the efficacy of conventional Ganirelex/Cetrotide injectables treatment for IVF in the 5 representative patients versus the Elagolix used in the kit described herein in the 5 representative patients. The results demonstrated that Elagolix showed excellent suppression of serum LH blood hormone levels.

Table 4 shows the age and the clinical outcome of women who underwent oocyte/embryo freezing using the At-HOME IVF kit. On the day of the oocyte retrieval, all patients had transvaginal ultrasound before the procedure and all follicles between 14-22 mm were considered “large” enough for puncture and collection. In all the participants, the number of large follicles that grew in response to the ovarian stimulation ranged from 1 to 8. According to the ultrasound results, none of the patients ovulated on the day of presentation for the oocyte retrieval. As seen in Table 4, all patients underwent oocyte retrieval with 21 out of 22 patients (95.45%) had at least one or more oocytes collected with the number of oocytes ranging from 1 to 7; one participant did not have any oocytes collected. Details on the number of immature oocytes including GV (germinal vesicle) and MI (metaphase I) are shown in Table 4. Eight out of 16 patients (50%) who underwent IVF had embryos cryopreserved at either the cleavage or blastocyst stage.

**Discussion**

This pilot study showed that the At-HOME IVF kit for oocyte/embryo freezing provides patients with the ability to limit the number of office visits during fertility treatment with an acceptable outcome. Further, because the oocyte/embryo freezing medications are administered in formulations that are not injectables (i.e., oral tablets, vaginal suppositories, and nasal sprays), patients can avoid the uncomfortable and painful injections used in traditional oocyte/embryo freezing medication regimens. Accordingly, the present kit provides a convenient, cost-effective, and pain-free medication regimen for patients seeking oocyte/embryo freezing during the COVID-19 pandemic or when time is of essence.

It has been recently suggested that, during the COVID-19 pandemic, the use of mild stimulation, GnRH antagonist control of the LH surge, GnRH agonist triggering, and single embryo transfer or freeze-all, are the first choice in this period for women entering IVF [6]; all of which are provided by the At-HOME IVF kit presented herein. For mild ovarian stimulation, the kit uses a combination of clomiphene citrate and letrozole; each of which works via a different mechanism to increase endogenous pituitary FSH hormone release. Indeed, recent data have shown that the combination of these two medications can yield great results with ovarian stimulation [13, 14]. For ovulation suppression, the kit uses the vaginal/oral GnRH antagonist pill Elagolix which showed in a pilot of 5 participants that it was able to suppress the LH serum level by up to approximately 88% (Table 3). Interestingly, vaginal Elagolix suppressed ovulation in 100% of the patients in our pilot, and the percentage of LH drop following vaginal Elagolix pill seems much higher than that observed with the traditional Ganirelex/Cetrotide injectable (Table 3). Larger scale studies are needed to compare the effectiveness of Elagolix pill to the traditional Ganirelex/Cetrotide injectable in the prevention of premature LH surge in IVF cycles. To our knowledge, only one study assessed the effect of Elagolix on ovulation suppression [10], however that study used a 28-day dose interval of Elagolix orally in order to mimic the intake the medication in women with endometriosis. Some studies have shown that medroxyprogesterone acetate (MPA) is effective as an oral treatment for the prevention of premature LH surge in IVF treatments [15-17]; however, we chose Elagolix over MPA for several reasons. First, the treatment protocols that uses MPA for the prevention of premature LH surge almost always require the use of injectable gonadotropins for ovarian stimulation [15-17] because MPA acts by inhibiting the hypothalamic-pituitary-ovarian (HPO) axis. Since the At-Home IVF kit relies on an intact HPO axis because it uses clomiphene citrate and letrozole for ovarian stimulation and because the kit does not contain the injectable gonadotropins, MPA was not a viable option for our kit. Second, most protocols that included MPA for the prevention of premature LH surge, have used HCG injection as a trigger for oocyte maturation due to
ceeding with fertility treatments with minimum exposure to office visits.

**Author Contribution**

Z.M. and J.Z. contributed to the literature search, drafting and revising the manuscript, and final approval of the submitted version.

**List of Abbreviations**

IVF, in vitro fertilization; DOR, diminished ovarian reserve; ASRM, American Society for Reproductive Medicine; IUI, intrauterine insemination; SART, society for assisted reproductive technology; AMH, anti-Müllerian hormone; ICSI, intracytoplasmic sperm injection; AFC, antral follicle count; FSH, follicle-stimulating hormone.

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**Conflict of Interest**

All authors have nothing to disclose.

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**References**

[1] Wang C., Horby P.W., Hayden F.G., Gao G.F.: "A novel coronavirus outbreak of global health concern". Lancet, 2020, 395, 470.
[2] https://www.asrm.org/news-and-publications/covid-19/.
[3] https://www.sart.org/professionals-and-providers/covid-19-resources/.
[4] https://www.eshre.eu/Press-Room/ESHRE-News.
[5] Rodriguez-Wallberg K.A., Wikander I.: "A global recommendation for restrictive provision of fertility treatments during the COVID-19 pandemic". Acta Obstet. Gynecol. Scand., 2020.
[6] La Marca A., Niederberger C., Pellicer A., Nelson S.M.: "COVID-19: lessons from the Italian reproductive medical experience". Fertil. Steril., 2020, 13, 920-922.
[7] Hernandez C., Valdera C.J., Cordero J., Lopez E., Plaza J., Albi M.: "Impact of telemedicine on assisted reproduction treatment in the public health system". J. Healthc. Qual. Res., 2020, 35, 27.
[8] Shebley M., Polepally A.R., Nader A., Ng J.W., Winzenborg I., Klein C.E., et al.: "Clinical Pharmacology of Elagolix: An Oral Gonadotropin-Releasing Hormone Receptor Antagonist for Endometriosis". Clin. Pharmacokinet., 2020, 59, 297.
[9] Taylor H.S., Giudice L.C., Lessey B.A., Kotarski J., Archer D.F., et al.: "Treatment of Endometriosis-Associated Pain with Elagolix, an Oral GnRH Antagonist". N. Engl. J. Med., 2017, 377, 28.
[10] Archer D.F., Ng J., Chwalisz K., Chiu Y.L., Feinberg E.C., Miller C.E., et al.: "Elagolix suppresses ovulation in a dose-dependent manner: results from a 3-month, randomized study in ovulatory women". J. Clin. Endocrinol. Metab., 2020, 105, dg0886.
[11] Ng J., Chwalisz K., Carter D.C., Klein C.E.: "Dose-Dependent Suppression of Gonadotropins and Ovarian Hormones by Elagolix in Healthy Premenopausal Women". J. Clin. Endocrinol. Metab., 2017, 102, 1683.
[12] El-Nemr A., Bhude M., Khalifa Y., Al-Mizyen E., Gillott C., Lower Z. Merhi, J. Zhang
A.M., et al.: "Clinical evaluation of three different gonadotrophin-releasing hormone analogues in an IVF programme: a prospective study". *Eur. J. Obstet. Gynecol. Reprod. Biol.*, 2002, 103, 140.

[13] Mejia R.B., Summers K.M., Kresowik J.D., Van Voorhis B.J.: "A randomized controlled trial of combination letrozole and clomiphene citrate or letrozole alone for ovulation induction in women with polycystic ovary syndrome". *Fertil. Steril.*, 2019, 111, 571.

[14] Hajishafiha M., Dehghan M., Kiarang N., Sadegh-Asadi N., Shayegh S.N., Ghasemi-Rad M.: "Combined letrozole and clomiphene versus letrozole and clomiphene alone in infertile patients with polycystic ovary syndrome". *Drug Des. Devel. Ther.*, 2013, 7, 1427.

[15] Kuang Y., Chen Q., Fu Y., Wang Y., Hong Q., Lyu Q., et al.: "Medroxyprogesterone acetate is an effective oral alternative for preventing premature luteinizing hormone surges in women undergoing controlled ovarian hyperstimulation for in vitro fertilization". *Fertil. Steril.*, 2015, 104, 62.

[16] Beguería R., García D., Vassena R., Rodriguez A.: "Medroxyprogesterone acetate versus ganirelix in oocyte donation: a randomized controlled trial". *Hum. Reprod.*, 2019, 34, 872.

[17] Dong J., Wang Y., Chai W.R., Hong Q.Q., Wang N.L., Sun L.H., et al.: "The pregnancy outcome of progestin-primed ovarian stimulation using 4 versus 10 mg of medroxyprogesterone acetate per day in infertile women undergoing in vitro fertilisation: a randomised controlled trial". *BJOG*. 2017, 124, 1048.

[18] Nargund G., Datta A.K., Fauser B.: "Mild stimulation for in vitro fertilization". *Fertil. Steril.*, 2017, 108, 558.

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