O-6 Monday, October 14, 2019 12:00 PM

PHASE 3 TRIAL RESULTS: EFFICACY AND SAFETY OF ELAGOLIX IN A SUBSET OF WOMEN WITH UTERINE FIBROIDS AND ADENOMYOSIS. Ozgul Muneyyirci-Delale, MD,[a] David F. Archer, MD,[b] Jin Hee Jeannie Kim, MD,[c] Ran Liu, PhD,[d] Charlotte D. Owens, MD,[d] Elizabeth E. Puscheck, MD, MS, MBA[e] [a]State University of New York, Brooklyn, NY; [b]Eastern Virginia Medical School, Norfolk, VA; [c]Columbia University, New York, NY; [d]AbbVie, Inc., North Chicago, IL; [e]Wayne State Uinversity, Detroit, MI.

OBJECTIVE: Adenomyosis is a benign lesion within the myometrium associated with heavy menstrual bleeding (HMB) and dysmenorrhea, and commonly co-exists with uterine fibroids (UF). Adenomyosis is also present in 15-57% of hysterectomy specimens with leiomyoma (Genc M, et al, 2015; Taran FA, et al, 2010). This analysis evaluated the efficacy and safety of elagolix, an oral, gonadotropin-releasing hormone receptor antagonist, with add-back therapy in a subset of women with UF, HMB and co-existing adenomyosis.

DESIGN: Data were pooled from two 6-month, randomized, double-blind, placebo-controlled phase 3 studies, Elaris UF-1 and UF-2. Premenopausal women (18-51 years) with ultrasound-confirmed diagnosis of UF and HMB (>80mL menstrual blood loss [MBL]/cycle) were randomized 1:1:2 to placebo, elagolix 300mg twice daily (BID), or elagolix 300mg BID with 1mg estradiol/0.5mg norethindrone acetate (E2/NETA) once daily.

MATERIALS AND METHODS: This subset analysis was conducted in women with HMB associated with UF and co-existing adenomyosis diagnosed by ultrasound and/or MRI at baseline (BL). The primary endpoint was the proportion of women with <80mL MBL during the final month and ≥50% reduction in MBL from BL to the final month. MBL and the diagnosis of HMB was assessed with the alkaline hematin method. Adverse events (AEs) were monitored.

RESULTS: Of 790 women treated, 16% had ultrasound and/or MRI diagnosed adenomyosis at BL. Pooled data demonstrated that the proportion of responders for the primary endpoint was significantly greater (P<0.001) for elagolix+E2/NETA [76.8% (95% CI, 65.84, 87.82)] compared to placebo [12.1% (95% CI, 0.97, 23.150)]. AEs reported in the adenomyosis subset included hot flushes, night sweats, headache, and nausea.

CONCLUSIONS: In women with HMB associated with UF and co-existing adenomyosis at BL, elagolix +E2/NETA significantly reduced MBL versus placebo similar to the all-subject group. AEs reported in this group were similar to the all subject group. These data suggest that further studies investigating the effect of elagolix in women with HMB associated with UF and adenomyosis may be warranted.

References: 1. Genc, M., et al., *Adenomyosis and accompanying gynecological pathologies.* Arch Gynecol Obstet. 2015. 291(4): p. 877-881.

2. Taran, F.A., et al., *Characteristics indicating adenomyosis coexisting with leiomyomas: a case-control study.* Human reproduction (Oxford, England). 2010. 25(5): p. 1177-1182.

SUPPORT: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

ART LAB: BASIC

O-7 Monday, October 14, 2019 10:45 AM

IMPLEMENTATION OF AN ELECTRONIC WHITEBOARD FOR QUALITY MANAGEMENT IN THE IN VITRO FERTILIZATION LABORATORY. Phillip A. Romanski, MD,[a] Ann M. Thomas, PhD,[b] Jay Patel, MS,[c] Dan Zhang, MD, PhD,[a] Catherine Racowsky, PhD[b] [a]Brigham & Women's Hospital and Harvard Medical School, Boston, MA; [b]Brigham & Women's Hospital, Boston, MA; [c]Brigham and Womens Hospital, Boston, MA.

OBJECTIVE: In 2014, we implemented an electronic whiteboard as a quality management tool to assist our embryologists to ensure their adherence to established standards for performing time-sensitive procedures (1). We aimed to test the hypothesis that use of an electronic whiteboard in the IVF laboratory increases the likelihood that critical evaluation procedures are performed within optimum pre-set time ranges.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Retrievals in our IVF clinic between 6/1/12 and 5/31/18 were included. The pre-electronic whiteboard time-period was 6/1/12 to 4/5/14, during which embryologists strived to adhere to the set optimum evaluation times but without a formal guide. The post-electronic whiteboard time-period was 3/1/15 to 5/31/18. The 13 months after the electronic whiteboard was introduced (4/6/14-2/28/15) were defined as a transition period and were excluded. Optimum pre-set time ranges were 16-18 hours post-insemination or ICSI (HPI) for the pronuclei (PN) check, 65-67 HPI for day 3 evaluations and 114-117 HPI for day 5 evaluations. Log binomial models estimated the risk ratio (RR, 95% confidence interval [CI]) of evaluations occurring within the optimum time ranges. Models were adjusted *a priori* for ICSI.

RESULTS: A total of 44,957 oocytes from 6,302 retrievals met inclusion criteria, of which 44.4% underwent ICSI. There were 16,434 oocytes from 2,703 retrievals pre-electronic whiteboard and 28,523 oocytes from 3,599 retrievals post-electronic whiteboard. The proportion of oocytes evaluated at the PN check within the optimum time range was statistically significantly increased after implementation of the electronic whiteboard (89.2% vs 80.8%, RR 1.11 [95% CI 1.10 – 1.12]). The proportion of day 3 and day 5 checks that occurred within the optimum time ranges were also statistically significantly increased after implementation of the electronic whiteboard (day 3: 73.3% vs 57.2%, RR 1.75 [95% CI 1.54 – 1.99]) and (day 5: 74.1% vs 58.8%, RR 1.26 [95% CI 1.24 – 1.29]).

CONCLUSIONS: Our findings indicate that use of an electronic whiteboard that posts optimum time ranges for performing critical IVF laboratory procedures tightens the actual evaluation times towards these ranges. Such improved standardization may lead to positive downstream effects on quality assurance analyses and embryo transfer and embryo cryopreservation management decisions. Future studies will investigate whether use of an electronic whiteboard in the IVF laboratory improves overall clinical care.

Reference: 1. Olofsson JI, Banker MR, Sjoblom LP. Quality management systems for your in vitro fertilization clinic's laboratory: Why bother? Journal of Human Reproductive Sciences. 2013;6:3.

SUPPORT: None.

O-8 Monday, October 14, 2019 11:00 AM

THE CLINICAL RESULTS OF PIEZO-ICSI COMPARED TO CONVENTIONAL-ICSI: A SIBLING-OOCYTE STUDY. Noriyuki Okuyama, M.Sc.,[a] Ryuichiro Obata, Ph.D.,[a] Nao Oka, M.Sc.,[a] Nobuya Aono, Ph.D.,[b] Tomoko Hashimoto, M.D., Ph.D.,[a] Koichi Kyono, M.D., Ph.D.[a] [a]Kyono ART Clinic Takanawa, Tokyo, Japan; [b]3-13-1, takanawa, Minato-ku, Tokyo, Japan.

OBJECTIVE: Clinically, conventional ICSI (CI) is a common, widely-used method, while there are few reports with respect to Piezo ICSI (PI). PI is effective in degeneration rate and fertilization rate (Kimura, Y & Yanagimachi, R, 1995). It is known that the survival rates of mice oocytes are low after CI; however, degeneration rate improved markedly using PI. PI is an effective technique for cases with fragile oocytes. It has been reported that the survival rate is similarly improved in human oocytes (Hiraoka, K & Kitamura, S, 2015). However, most of the studies reporting on PI are retrospective studies. Here, we prospectively compared the degeneration rates, fertilization rates and embryo development of PI and CI in a sibling study.

DESIGN: This is a prospective randomized controlled single-center study, using sibling oocytes, conducted from August 2018 to March 2019. Written informed consent was obtained from all patients involved in this study.

MATERIALS AND METHODS: This sibling oocyte study comprised 26 cycles in 26 cases. CI was performed in 149 mature oocytes. CI consists of mechanical penetration of the zona pellucida, breaking the oocyte membrane by aspiration of cytoplasm. PI was performed in 162 mature oocytes. PI consists of breaking the oocyte membrane and zona pellucida by Piezo pulse. P-value of 0.05 or less was considered to be statistically significant.ã€€€Limitation: The clinical results using vitrified oocytes, artificial oocyte activation, cryptozoospermia, azoospermia cases, and females aged over 40 years old were not included in this study. The pregnancy outcome has not been confirmed in our study.

RESULTS: There were no statistically significant differences in the fertilization rates, degeneration rates, cleavage rates, blastocyst formation rates or good quality blastocyst rates (according to the Gardner criteria) between CI and PI (75.8% vs. 78.4% (P=0.592), 7.4% vs. 3.7% (P=0.146), 100% vs. 96.8% (P=0.160), 61.9% vs. 64.0% (P=0.743) and 41.6% vs. 36.8% (P=0.450), respectively).

CONCLUSIONS: In conclusion, the present study has demonstrated there was no significant difference in the clinical results of piezo-ICSI and conventional-ICSI. However, this may be attributable to the limited number of cases with fragile oocytes, etc. In our experience, PI is safer and easier to learn and

perform in clinical work in a shorter period, especially for beginners. Further studies are necessary.

Group	Conventional ICSI	Piezo ICSI	P
Patients (N)	26		-
No. of ICSI cycles	26		-
Female age, years (mean ± SD)	34.8 ± 4.2		-
Male age, years (mean ± SD)	36.9 ± 5.4		-
No. of oocytes	149	162	-
N(%) of zygotes (2PN)	113 (75.8)	127 (78.4)	0.592
N(%) of degenerated oocytes	11 (7.4)	6 (3.7)	0.146
N(%) of cleaved oocytes	113 (100)	122 (96.8)	0.167
N(%) of blastocysts	70 (61.9)	80 (64.0)	0.477
N(%) of good quality blastocysts	47 (41.6)	46 (36.8)	0.498

O-9 Monday, October 14, 2019 11:15 AM

WOULD AN AUTOMATED SYSTEM DETECTING EMBRYO DEVELOPMENTAL EVENTS SELECT THE SAME EMBRYO AS AN EMBRYOLOGIST USING A MORPHOKINETIC ALGORITHM?. Raquel Del Gallego, PhD,[a] Lorena Bori Arnal, PhD,[a] Lucia Alegre, PhD,[a] Teija Peura, PhD,[b] Manuel Ugidos, PhD,[c] Marcos Meseguer, PhD[d] [a]IVIRMA Global, Valencia, Spain; [b]Genea Biomedx, Sydney, NSW, Australia; [c]Instituto de Biomedicina de Valencia, Valencia, Spain; [d]IVIRMA Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: The objective of this study is to compare embryo grading and clinical result prediction obtained with a morphokinetic algorithm using an automated system for embryo developmental events annotations vs. manual annotations performed by an embryologist team.

DESIGN: Retrospective study including morphokinetic manual and automated data from 1,370 embryos (284 patients) at IVIRMA Valencia clinic. All embryos were normally fertilized embryos cultured up to day 5/6. All were included regardless of their treatment (egg donation or autologous), oocyte origin (fresh or frozen) or patient age (range: 27-44 years).

MATERIALS AND METHODS: All embryos were annotated manually by a busy embryologist team in the routine clinical practice using Geri Assess® 1.3 software (IVI). The same videos were retrospectively assessed by the stand-alone Geri Assess® 2.0 software (GA2), including filtration of events falling outside the pre-defined time-ranges, as is done in the full Geri system. Both morphokinetic manual and automated annotations went through an embryo selection algorithm developed by Basile *et al.* (2015) considering the morphokinetic parameters **t3**, **cc2** (t3-t2) and **t5**. Embryos were graded and the accuracy in the prediction was assessed between both groups in terms of embryo outcome, bHCG test, and fetal heartbeat. Data was statistically analyzed with chi-squared and binomial proportion tests.

RESULTS: High accordance was found between IVI and GA2 embryo grading through Basile's algorithm. Out of the 1,370 embryos, 1,045 were utilized as transferred or vitrified, showing no statistically significant differences between both groups in all grades: A+, A, B+, B, C+, C, D+ and D; except for No Grade ($p < 0.05$). More ungraded embryos were found in the automated group, as Geri Assess® 2.0 is designed to eliminate events falling outside of pre-defined time-ranges, these annotations being considered anomalous. **t3** was the most unavailable parameter in the GA2 data. Regarding only the 391 KID transferred embryos, bHCG test and fetal heartbeat data also did not show statistically significant results between IVI and GA2. Previous studies in our group have proven a high GA2 detection rate in the great majority of the events, especially in early cleavage divisions, which explains its good performance with the algorithm parameters: **t3**, **cc2** and **t5**.

CONCLUSIONS: The results of the study support the use of automated systems for embryo morphokinetic annotations. This non-invasive and objective tool standardizes the annotating process avoiding inter- and intra-grader variability, in addition to facilitating the routine clinical practice. The establishment of automation would need a gradual transition controlled by lab professionals, as yet chaotic embryos or artifacts in the well hinders its performance.

References: Basile N, Vime P, Florensa M, Aparicio Ruiz B, García Velasco JA, Remohí J, Meseguer M. The use of morphokinetics as a predictor of implantation: A multicentric study to define and validate an algorithm for embryo selection. Hum Reprod 2015; 30:276–283.

SUPPORT: Predoctoral Generalitat Valenciana and European Social Fund.

O-10 Monday, October 14, 2019 11:30 AM

PROPORTION OF PATIENTS DETECTED WITH SUBCLINICAL HYPOTHYROIDISM IS INDEPENDENT OF TIME OF BLOOD DRAW. Christine Briton-Jones, PhD, HCLD,[a] Jenna Friedenthal, MD,[b] Sydney Chang, MD,[b] Taraneh Gharib Nazem, MD,[b] Dmitry Gounko, MA,[a] Joseph A. Lee, BA,[a] Alan B. Copperman, MD[b] [a]Reproductive Medicine Associates of New York, New York, NY; [b]Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: There are differences in clinical opinion regarding the benefit of treating subclinical hypothyroidism in infertile patients. However, for patients with a thyroid stimulating hormone (TSH) serum level > 2.5mIU/L it is recommended to continue monitoring or administer levothyroxine to reduce TSH serum levels <2.5mIU/L (ASRM guideline document 2015). TSH levels in adults, have a predictable circadian rhythm, with the highest levels produced between 2am and 4am; while the lowest levels occur between 4pm and 8pm. Whether there is a misdiagnosis of subclinical hypothyroidism and underlying normal circadian rhythm due to testing afternoon blood draw is a current clinical concern. Only one study has showed the potential for this misdiagnosis, albeit the study included a small sample size. [1] The objective of this study was to identify any differences in the mean TSH levels obtained from morning compared to afternoon blood draws in patients seeking infertility treatment.

DESIGN: Retrospective cohort analysis

MATERIALS AND METHODS: This study examined patients having routine TSH levels tested for either cycle day 3 evaluations or as part of a new patient consultation from January 2018 and March 2019. Serum TSH concentrations were obtained via electrochemiluminescence immunoassay Elecsys for use on Cobas e601(Roche) Detection range of 0.005 – 100 mIU/L. Chi Square analysis was used to determine statistical significance with $p<0.05$ considered significant.

RESULTS: Of the 8345 patients who had routine TSH testing performed, 5028 were drawn in the morning and 3281were drawn in the afternoon. There was no significant difference in the mean (± SD) TSH levels, 2.10408 (4.30) for am blood draws and 2.10426 (4.31) for pm blood draws. There was also no differences in the in the percentage of TSH results showing >2.5mIU/L in morning 25% compared to afternoon blood draw groups 26%.

CONCLUSIONS: This study showed no shift in the mean or in percentage of patients with elevated TSH levels in the morning compared to afternoon blood draw group. This data shows that afternoon blood draws are just as likely to detect elevated TSH levels as blood samples drawn in the morning. The strength of this study is its ability to define risks of misdiagnosis of subclinical hypothyroidism due to potential underlying changes in TSH levels for the different times of blood draw using binomial sorting of patient data in a diverse population of patients seeking ART treatment. This study highlights how TSH fluctuations that may occur throughout the day are clinically insignificant and even with ultra-sensitive immunoassays not, detectable in a population of patients undergoing reproductive treatment.

Reference: Roelfsema F. and Veldhuis JD. Thyrotropin secretion patterns in health and disease. Endocrinology Reviews. 2013 34(5): 619-57.

SUPPORT: None.

O-11 Monday, October 14, 2019 11:45 AM

PRELIMINARY RESULTS FROM THE FIRST REGISTERED PILOT TRIAL WITH MATERNAL SPINDLE TRANSFER TO OVERCOME INFERTILITY. Nuno Costa-Borges, PhD,[a] Eros Nikitos, MSc,[b] Katharina Spath, PhD,[c] Dagan Wells, PhD,[c] Klaus Rink, PhD,[a] Yannis Vasilopoulos, MD,[d] Ioannis Zervomanolakis, MD,[b] Dimitropoulos Konstantinos, MD,[b] Polyzos Panagiotis, MD,[b] Stylianos Grigorakis, MD, FRCOG,[b] George Kontopoulos, MD,[b] Konstantinos Kostaras, MD, PhD,[d] Panagiotis S. Psathas, MD,[d] Gloria Calderón, PhD[a] [a]Embryotools, Barcelona, Spain; [b]Institute of Life, Athens, Greece; [c]IVI RMA, Oxford, United Kingdom; [d]Institute of Life, Atherns, Greece.