O-70 Monday, October 8, 2018 11:30 AM

INDIVIDUALIZATION OF THE STARTING DOSE OF GONADOTROPIN REDUCES THE OVERALL OHSS RISK AND THE NEED OF PREVENTIVE INTERVENTIONS: CUMULATIVE DATAOVERTHREE STIMULATION CYCLES.

M. Fernandez-Sanchez,[a] H. Visnova,[b] A. A. Yuzpe,[c] B. M. Klein,[d] B. Mannaerts,[d] J. C. Arce.[e] aIVIRMA Sevilla, Sevilla, Spain; bIVF CUBE, SAR CGPS, Prague, Czech Republic; cOlive Fertility Centre, Vancouver, BC, Canada; dFerring Pharmaceuticals, Copenhagen, Denmark; eFerring Pharmaceuticals, Parsippany, NJ.

OBJECTIVE: To evaluate the impact of individualized dosing with follitropin delta in sequential controlled ovarian stimulation (COS) cycles as a preventive strategy for OHSS risk.

DESIGN: A combined analysis of two large comparative Phase 3 trials of follitropin delta.

MATERIALS AND METHODS: Secondary analysis of three stimulation cycles in IVF/ICSI patients included in a randomized, assessorblinded trial comparing two recombinant FSH preparations (ESTHER- 1, NCT01956110), and undergoing up to two additional COS cycles while maintaining the same treatment allocation and the assessor-blinded design (ESTHER-2, NCT01956123). A total of 1326 women were randomized in COS cycle 1 and treated with follitropin delta (Rekovelle_) or follitropin alfa (Gonal-f_). Of these, 513 continued to cycle 2 and 188 to cycle 3. In COS cycle 1, the individualized follitropin delta dosing regimen was a fixed daily dose determined by serum AMH and body weight, and the conventional follitropin alfa dosing regimen was 150 IU for the first 5 days after which the daily dose could be adjusted. In COS cycles 2 and 3, the FSH doses were maintained or adjusted according to the ovarian response in the previous cycle.

RESULTS: Individualized dosing with follitropin delta resulted in a significant reduction in moderate/severe OHSS and/or preventive interventions (OR¼0.59 [0.38; 0.92], p¼0.018) compared to conventional dosing approach with follitropin alfa in patients undergoing up to three COS cycles. The greatest benefit was observed in the patients in the highestAMH quartile (R25.35 pmol/L; OR¼0.47 (0.26; 0.86); p¼0.012). When evaluating OHSS cases and the preventive interventions separately, individualized dosing with follitropin delta was associated with a significantly lower incidence of moderate/ severe OHSS (OR¼0.50 [0.26; 0.97], p¼0.036) and a significantly lower incidence of preventive interventions (OR¼0.56 [0.31; 0.99], p¼0.044), mainly GnRH agonist triggering with no fresh transfer, compared to the conventional dosing approach with follitropin alfa. Across the three cycles, two women were hospitalized due to

OHSS in the individualized follitropin delta dosing group compared to eight in the conventional follitropin alfa dosing group.

CONCLUSIONS: Individualized follitropin delta dosing decreases risk of moderate/severe OHSS and preventive interventions compared with conventional follitropin alfa treatment, mainly in patients with highest serum AMH.
Supported by: Ferring Pharmaceuticals.