

Reproductive Endocrinology

Monday, June 26<sup>th</sup>

Poster area

## SESSION TYPE

Poster viewing

## ABSTRACT TITLE

**P-679: CONTROLLED OVARIAN STIMULATION USING FOLLITROPIN DELTA RESULTS IN HIGHER CUMULATIVE LIVE BIRTH RATE COMPARED TO FOLLITROPIN ALFA/BETA IN A LARGE PROSPECTIVE REAL WORLD DATASET.**

## BIOGRAPHY

Dr. Alexander Freis studied at the Universities Freiburg, Zurich and Lausanne. He joined the department of Gynecologic Endocrinology and Fertility Disorders in Heidelberg in 2016, representing the largest academic IVF-center in Germany. Since 2020, he is member of KINDERWUNSCH Erlangen, a private fertility clinic but continues his research and lectures at the universities Heidelberg and Erlangen. His main research areas are biomarkers in reproductive medicine as well as reproductive endocrinology, implantation, endometrium and early embryo development

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## Study question:

Does IVF/ICSI-treatment using follitropin delta (hrFSH) result in higher pregnancy rates (PR) or live birth rates (LBR) compared to follitropin alfa/beta (recFSH)?

## Summary answer:

Real world data (RWD) from a large prospective German registry study shows that using hrFSH results in higher pregnancy rates compared to recFSH.

## What is known already:

Follitropin delta represents a new recombinant FSH derived from a human cell line. Contrary to follitropin alfa or beta, follitropin delta has a glycolysation pattern consisting of  $\alpha$ 2,3- and  $\alpha$ 2,6-linked sialic acids which is more similar to native human FSH. Follitropin delta is approved for use with an individualized dosing algorithm based on serum AMH and body weight, targeting an optimal ovarian response (8-14 oocytes). Efficacy and safety have been demonstrated in numerous clinical trials.

Moreover, Follitropin delta seems to reduce the risk of OHSS although its safety with respect to ovarian hyperstimulation using RWD remains to be investigated.

#### **Study design, size, duration:**

The German IVF Registry collects prospectively data about IVF/ICSI-treatments from 140 German IVF centers. The underlying analysis of RWD includes controlled ovarian hyperstimulation cycles that have been performed in Germany between 2017-2021. Study groups were built subject to the gonadotropin used for stimulation, irrespective of previous treatments: (1) hrFSH, n=3002, (2) recFSH, n=135293. "Pregnancy" was defined as clinically assessed, intrauterine pregnancy, including miscarriages. Biochemical pregnancies were not defined as "pregnant". Ectopic pregnancies (n=558) were excluded.

#### **Participants/materials, setting, methods:**

PR and LBR were calculated subject to the number of embryo transfers (ET) (n=2062 (hrFSH) vs. n=103357 (recFSH)) after excluding freeze-all cycles, (n=529 (hrFSH) vs. n=13682 (recFSH)) and cycles that ended without ET (n=411 (hrFSH) vs. n=18254 (recFSH)). The collected data were saved in compliance with the applicable data processing regulations. Statistical analysis was performed using Fishers-exact- and students-t-test and Microsoft Excel, whereas  $p < 0.05$  was defined as significant.

#### **Main results and the role of chance:**

There was no difference between the study groups regarding age ( $33.9 \pm 4.00y$  (hrFSH) vs.  $33.8y \pm 4.34y$  (recFSH),  $p=0.12$ ) or infertility diagnosis. Stimulation with hrFSH resulted in a higher number of oocytes ( $11.15 \pm 7.2$  vs.  $10.39 \pm 7.01$ ,  $p < 0.01$ ). Antagonist protocol was used less often in the hrFSH-group (78% (2344/3002) vs. 80% (109217/135293),  $p < 0.01$ ). PR in 2021 were higher (39.2% (222 pregnancies / 567 embryo transfers) vs. 35.2% (6837/19420), OR= 1.18 [0.99-1.41]  $p=0.05$ ) while using hrFSH compared to recFSH. The effect was even stronger when comparing patients aged 30-34y (46.2% (98/212) vs. 38.6% (2967/7865), OR= 1.41 [1.07-1.88],  $p=0.01$ ). Another quantitative difference could be observed for patients aged 30-34y in their first IVF/ICSI-cycle (PR 48.5% (63/130) vs. 39.5% (1926/4873), OR= 1.44 [1.00-2.07],  $p=0.05$ ). Including all cycles between 2017-2021 resulted in higher PR for couples treated with hrFSH (38.3% (790/2062) vs. 36.2% (37439/103357), OR= 1.09 [1.00-1.20],  $p=0.049$ ). Cumulative PR including consecutive frozen embryo transfers after the first stimulation showed significantly higher PR while using hrFSH (81.6% (422/517) vs. 71.3% (17373/24367), OR= 1.79 [1.42-2.23],  $p < 0.01$ ). Finally, cumulative LBR per ET was significantly increased if hrFSH was used for ovarian stimulation (60.0% (310/517) vs. 51.9% (12648/24367), OR= 1.39 [1.16-1.66],  $p < 0.01$ ) compared to recFSH.

#### **Limitations, reasons for caution:**

Since we analyzed RWD, comparison with large clinical trials should be considered carefully. PR and LBR was calculated only using stimulations which successfully generated ET. Moreover, individual AMH values are not transmitted to the German IVF Registry. Therefore, difference in ovarian reserve between study groups can't be excluded.

**Wider implications of the findings:**

In this large, prospective RWD, higher cumulative LBR and PR using hrFSH compared to recFSH, irrespective of age or infertility diagnosis, supports the use of individualized fertility treatment approach based on hrFSH. These results are consistent with previous retrospective findings.