Session 43: New Concepts: Ovarian Stimulation

Tuesday, June 27th, 10:00 - 11:15, Hall D1

Hall D1

SESSION TYPE

Selected oral communication

ABSTRACT TITLE

O-131: BEYOND: A RANDOMISED CONTROLLED TRIAL COMPARING EFFICACY AND SAFETY OF INDIVIDUALISED FOLLITROPIN DELTA DOSING IN GNRH AGONIST VERSUS ANTAGONIST PROTOCOLS FOR FIRST OVARIAN STIMULATION CYCLE (10:15 - 10:30)

PRESENTED BY:

Dr Soerdal

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BIOGRAPHY

Dr Soerdal is the founder and Medical Director of Medicus group, and works as specialist in assisted reproduction at the Medicus clinic in Trondheim, Norway. He trained as doctor at the University of Oslo, Norway, and as specialist in Gynecology and Obstetrics at the University Hospital of Trondheim, where he later trained and worked as specialist in assisted reproduction for 10 years, before opening his private IVF clinic in 2002. Over the course of his career, Dr Soerdal has been an investigator in more than 40 local, national or international clinical trials, including the BEYOND trial.

ABSTRACT TEXT

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Study question:

How does a long GnRH agonist versus a GnRH antagonist protocol affect ovarian response when using individualised fixed daily follitropin delta dose for ovarian stimulation?

Summary answer:
BEYOND trial data demonstrates that individualised follitropin delta dosing is safe and effective in a long GnRH agonist protocol in women with AMH ≤35 pmol/L.

What is known already:
Efficacy and safety of a fixed daily dose of follitropin delta, individualised based on bodyweight and anti-Müllerian (AMH), have been established in RCTs using a GnRH antagonist protocol. Preliminary study data shows that individualised follitropin delta is efficacious when used with a long GnRH agonist protocol (RAINBOW trial). There is no comparative data for efficacy and safety of individualised follitropin delta in a long GnRH agonist versus an antagonist protocol.

Study design, size, duration:
This was a randomised, controlled, open-label, multi-centre trial comparing efficacy and safety of individualised follitropin delta dosing in a long GnRH agonist versus an antagonist protocol in participants undergoing their first ovarian stimulation for IVF/ICSI conducted between May 2019 and February 2022. The primary endpoint was the number of oocytes retrieved. Important secondary endpoints included ongoing pregnancy rates and adverse drug reactions, with a special focus on OHSS. A total of 437 participants were randomised.

Participants/materials, setting, methods:
Participants, 18–40 years old with AMH ≤35 pmol/L, were enrolled at specialist reproductive health clinics in Austria, Denmark, Israel, Italy, the Netherlands, Norway and Switzerland. The mean number of oocytes retrieved was compared between the agonist and antagonist protocols using a negative binomial regression model with age and AMH at screening as factors. The analyses were based on all randomised subjects, using a multiple imputation method for randomised subjects withdrawing before start of stimulation.

Main results and the role of chance:
Of the 437 randomised subjects, 202 and 204 initiated ovarian stimulation with follitropin delta in the agonist and antagonist groups, respectively. Baseline mean data were: age, 32.3±4.3 years; AMH, 16.6±7.8 pmol/L, respectively. The number of oocytes retrieved was statistically significantly higher in the agonist (11.1±5.9) versus antagonist (9.6±5.5) group, with an estimated mean difference of 1.31 oocytes (95% CI: 0.22; 2.40, p=0.0185). The difference in number of oocytes retrieved was influenced by the patients' age and ovarian reserve, with a greater difference observed in patients <35 years and patients with high ovarian reserve (AMH >15 pmol/L). Cycle cancellations (2.0% versus 3.4%) and transfer cancellations (13.7% versus 14.7%) were similar in both groups. Ongoing pregnancy rate (36.9% vs 29.1%; estimated difference: 7.74% [95% CI: −1.49; 16.97, p=0.1002]) and other pregnancy outcomes were higher in the agonist versus antagonist protocol group, but the differences were not statistically significant. The most commonly reported adverse events (≥1% in either group) were similar in both groups (headache, OHSS, nausea, pelvic pain or discomfort, and abdominal pain). Incidence of early moderate/severe OHSS was low (1.5% versus 2.5%). Early pregnancy loss was similar between the groups (20% vs 24% of subjects with positive beta-hCG test, respectively).

Limitations, reasons for caution:
Subjects with AMH >35 pmol/L were not enrolled. Clinicians should remain cautious when using a GnRH agonist protocol in patients with AMH >35 pmol/L (greater OHSS risk). OHSS incidence in the GnRH antagonist group may have been lower if a GnRH agonist trigger had been allowed.

Wider implications of the findings:
In women with AMH ≤35 pmol/L, a fixed daily dose of follitropin delta (individualised according to bodyweight and AMH) showed similar efficacy when used in a long GnRH agonist protocol with no additional safety signals observed and no additional risk of OHSS versus follitropin delta used in an antagonist protocol.