Safety and Quality in ART

Monday, June 26th

Poster area

SESSION TYPE

Poster viewing

ABSTRACT TITLE

P-761: LIVE-BIRTH AND NEONATAL OUTCOMES FROM BEYOND, A RANDOMISED CONTROLLED TRIAL COMPARING EFFICACY AND SAFETY OF INDIVIDUALISED FOLLITROPIN DELTA DOSING IN GNRH AGONIST VERSUS ANTAGONIST PROTOCOLS

BIOGRAPHY

Anja Pinborg is specialist in reproductive medicine and medical director and professor at the Fertility Department at Rigshospitalet, Copenhagen University Hospital in Copenhagen, Denmark. Her research activities include clinical trials, quality and safety in ART, reproductive epidemiology and children follow-up. She has been ESHRE national representative for Denmark and was Medical advisor of the ESHRE steering committee of nurses and midwifes certification (2013 to 2017) and ESHRE EXCO member (2017-2021). She is past chairman for the Nordic Fertility Society (2011-2016) and has been associate editor for Human Reproduction Update. She is past EIC for the Danish Medical Journal and board member of the International Committee of Medical Journal Editors (ICMJE). She is principal investigator in the Reprounion collaboration and member of the steering committee of CoNARTaS (Committee of Nordic ART and Safety) a Nordic database on all children born after ART the last 30 years. She is very passionate about improving clinical reproductive medicine with focus on risks and safety aspects and solutions making it possible to survey short and long term outcomes in children born after ART on an international basis. She has written more than 250 scientific papers.

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Study question:

What are the live birth and neonatal outcomes following an individualised follitropin delta dosing regimen in either a long GnRH agonist or GnRH antagonist protocol?

Summary answer:
Live birth rates and neonatal outcomes were similar, supporting the efficacy and safety of follitropin delta in both GnRH agonist and antagonist protocols.

What is known already:
Follitropin delta is used for ovarian stimulation and is administered as a fixed daily dose, individualised based on bodyweight and anti-Müllerian (AMH) levels. Registrational trials for follitropin delta used a GnRH antagonist protocol. Preliminary study data shows that individualized follitropin delta is efficacious when used with a long GnRH agonist protocol (RAINBOW trial); however, there is no comparative data for the effects on live birth rates and neonatal outcomes with individualised follitropin delta in a long GnRH agonist versus an antagonist protocol.

Study design, size, duration:
This RCT compared the efficacy and safety of individualised follitropin delta dosing using a long GnRH agonist versus an antagonist protocol and was conducted between May 2019 and February 2022. The trial was designed to describe potential differences in the number of oocytes retrieved between the two GnRH analogue protocols (reported separately). A total of 437 participants were randomised, with a post-trial follow-up period to 4 weeks after birth to record birth and neonatal outcomes.

Participants/materials, setting, methods:
Participants were 18–40 years old with AMH ≤35 pmol/L, undergoing their first ovarian stimulation cycle for IVF/ICSI at specialist reproductive health clinics in Austria, Denmark, Israel, Italy, the Netherlands, Norway and Switzerland.Live birth rates were compared using a logistic regression model with age and AMH at screening as factors. Multiple imputation was used for randomised subjects withdrawing before start of stimulation. Subjects with transfer cancellation due to COVID-19 related reasons were excluded.

Main results and the role of chance:
All participants had a single blastocyst transferred, except two participants ≥38 years in the agonist group who received a double transfer resulting in one dichorionic diamniotic pregnancy for one subject, complicated by maternal hypertension and preterm birth at 33 weeks. All 133 participants with ongoing pregnancies (138 fetuses) were included in this post-trial follow-up analysis. Late pregnancy losses (after confirmed ongoing pregnancy) were similar in the agonist and antagonist groups (2.7% and 1.7%). There were 130 live births (agonist group: 75 neonates [67 singletons; 4 sets of twins]; antagonist group: 60 neonates [58 singletons; 1 set of twins]). Estimated live-birth rates were 35.8% and 28.7% in the agonist and antagonist groups, respectively, per started cycle (treatment difference 7.15%; 95% CI: –2.02; 16.31; p=0.1265). There were two neonatal deaths in the agonist group – a set of monochorionic twins born at gestational age 24 weeks + 2 days died shortly after birth due to prematurity. The two treatment groups were

comparable with respect to neonatal health data for singletons and twins, and incidence of congenital malformations (2.7% and 3.3%, respectively). Neonatal admissions to intensive care units were similar for both groups (10 and six neonates, respectively).

Limitations, reasons for caution:
Double blastocyst transfer was permitted for participants ≥38 years with no good-quality blastocysts. Neonatal health is dependent on singleton/twin status. Outcomes of transfers with cryopreserved blastocysts were not followed up – the cumulative live birth rates and neonatal outcomes after cryo-transfer are not known.

Wider implications of the findings:
The safety profile of individualised follitropin delta dosing was similar in GnRH agonist and antagonist protocols. Live birth rates following individualised follitropin delta were also similar for both GnRH protocols. There were no safety concerns with respect to the neonatal health after ovarian stimulation with follitropin delta.