Evaluation of FE 999049 Dosing Suitability in United States (US) Women Undergoing Controlled Ovarian Stimulation, a RITA Trial Analysis

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PURPOSE & OBJECTIVES

- FE 999049 is a human cell line-derived recombinant follicle-stimulating hormone (rFSH; **follitropin delta**) for controlled ovarian stimulation
- Greater potency of follitropin delta indicated that traditional rFSH dosing in IUs does not accurately reflect bioactivity; therefore, **follitropin delta is dosed in micrograms**[1-4]
- An individualized follitropin delta dosing regimen was established in a global program[5-8]
- The US RITA-1 and RITA-2 trials used a **flexible dosing regimen based on subject age**, with starting dosages based on data from the global program[9]
- **Objective:** Examine the suitability of the age-based, flexible follitropin delta dosing regimen used in the RITA trials

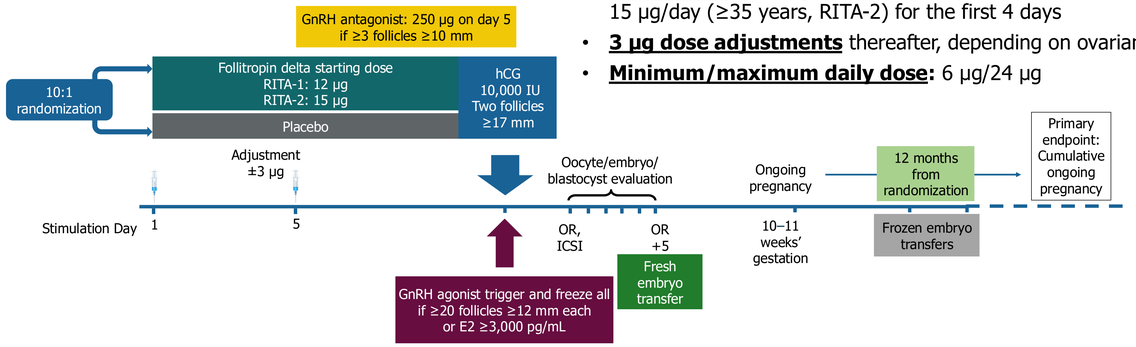
MATERIALS & METHODS

- **RITA-1 and RITA-2:** randomized, double-blind, placebo-controlled, parallel group, multicenter trials conducted at 24 US centers from 2018 to 2020
- Included 578 women 18-34 years of age (RITA-1) and 587 women 35-42 years of age (RITA-2)
- **RITA Trial Design (Figure)**
  - Randomized 10:1 to follitropin delta or placebo for ovarian stimulation in a gonadotropin-releasing hormone (GnRH) antagonist cycle
  - Age-based follitropin delta starting doses and flexible 3 µg dose adjustments after day 4
- **Primary efficacy endpoint:** cumulative ongoing pregnancy rate after fresh and frozen cycles initiated within 12 study months from the start of ovarian stimulation
- Early ovarian hyperstimulation syndrome (OHSS ≤9 days after trigger) was recorded as an adverse event

CONCLUSIONS

- The RITA trials confirmed the suitability of age-based follitropin delta starting doses with individualized dose adjustments

RITA TRIAL DESIGN



Ovarian Stimulation Protocol with Follitropin Delta

- **Starting dose:** 12 µg/day (<35 years, RITA-1) or 15 µg/day (≥35 years, RITA-2) for the first 4 days
- **3 µg dose adjustments** thereafter, depending on ovarian response
- **Minimum/maximum daily dose:** 6 µg/24 µg

RESULTS

Dosing (Table)

- Average duration of stimulation: 8 days
- On stimulation Day 5, more than half of the patients who received follitropin delta had no change in dose

Efficacy and Safety

Cumulative ongoing pregnancy rate after 12 months:
RITA-1: 64.0% (95%CI 56.9%-68.1%)
RITA-2: 43.9% (95%CI 37.0%-48.2%)

Moderate/severe early OHSS in fresh cycles:
RITA-1: 1.9%
RITA-2: 0.8%

No pregnancies or OHSS in the placebo group

Follitropin delta Dosing in RITA-1 and RITA-2

	RITA-1 FE 999049 (N=525)	RITA-2 FE 999049 (N=533)
Mean duration of gonadotropin treatment, days (SD)	8.1 (1.4)	8.2 (1.4)
Mean total gonadotropin dose, µg (SD)	104.2 (25.3)	131.2 (30.8)
Mean daily dose, µg/day (SD)	12.8 (1.4)	16.0 (1.4)
Investigator-requested dose changes on stimulation Day 5 (n, %)		
Decrease	33 (6.3%)	33 (6.2%)
No change	293 (55.8%)	270 (50.7%)
Increase	199 (37.9%)	230 (43.2%)

KEY TAKEAWAYS

- RITA-1 and RITA-2 confirmed the suitability of age-based microgram dosing of the rFSH follitropin delta
- Age-based starting doses and individualized dose adjustments achieved high cumulative ongoing pregnancy rates with low risk of OHSS
- More than half of patients did not require follitropin delta dose adjustments during ovarian stimulation

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