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Real-world Effectiveness and Safety of Follitropin Delta for Ovarian Stimulation: An Overview of Three Prospective Observational Studies

Enrica Gravotta,[1*] Christophe Blockeel,[2] Georg Griesinger,[3] Alexander Quaas,[4] Anja Pinborg,[5] Géraldine Porcu-Buisson,[6] Anne Guivarc'h-Levêque,[7] Ali Falahati,[8] Rita Lobo[1]

[1]Global Research and Medical, Ferring Pharmaceuticals, Kastrup, Denmark; [2]Brussels IVF, Centre for Reproductive Medicine, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Brussels, Belgium; [3]Department of Gynecological Endocrinology and Reproductive Medicine, University Hospital of Schleswig-Holstein, Luebeck, Germany; [5]Division of Reproductive Medicine and Gynecological Endocrinology, University Hospital Basel, Basel, Switzerland; [6]Fertility Clinic, Department of Gynecology, Fertility and Obstetrics, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark; [7]Department of Reproductive Medicine, Institut de Médecine de la Reproduction, Marseille, France; [7]Department of Reproductive Medicine, La Sagesse Clinic, Rennes, France; [8]Biometrics, Ferring Pharmaceuticals Co., Ltd, Tokyo, Japan. *Presenting author

OBJECTIVE

To summarise real-world effectiveness and safety of follitropin delta across three prospective observational studies spanning Europe, Canada and Australia

KEY TAKEAWAYS

1. **Consistent outcomes were observed across the three independent prospective real-world studies, highlighting the clinical relevance of the follitropin delta dosing algorithm**
2. **The majority of patients achieved the targeted 8–14 oocyte range, confirming real-world performance of the individualised dosing algorithm**
3. **RWE across diverse infertile populations, including patients with anovulatory PCOS, supports the effectiveness and safety of the follitropin delta dosing algorithm, reinforcing its applicability in routine clinical practice**

BACKGROUND

- The efficacy and safety of follitropin delta, using an individualised dosing algorithm based on serum anti-Müllerian hormone (AMH) and bodyweight, have been established in a global program of phase III randomised controlled trials (RCTs);[1-4] however, RCTs may not always reflect the vast diversity of patients seen in specialist reproductive health clinics
- Real-world evidence (RWE) is needed to confirm the effectiveness and safety of algorithmically dosed follitropin delta in clinical practice. Here, we summarise real-world evidence (RWE) for follitropin delta from prospective studies

METHODS

- Data were summarised from three prospective observational studies (PROFILE [Mar-2018 to Oct-2020], DELTA [Jun-2020 to Jun-2021] and NORSOS [Aug-2022 to Mar 2024)[5-7] that evaluated follitropin delta in women aged ≥18 years who were IVF/ICSI treatment-naïve (PROFILE and NORSOS) or undergoing their first or second IVF/ICSI cycle (DELTA)
- PROFILE was conducted in Belgium, the Netherlands, Germany, Italy, Australia, Austria, Canada, Poland, Spain and United Kingdom. DELTA was conducted in France. NORSOS was conducted in Denmark, Norway, Sweden and Switzerland
- We report baseline characteristics, follitropin delta exposure, ovarian responses, pregnancy outcomes, ovarian hyperstimulation syndrome (OHSS) and preventive treatments for early OHSS for one ovarian stimulation cycle. No formal statistical comparisons were performed

RESULTS

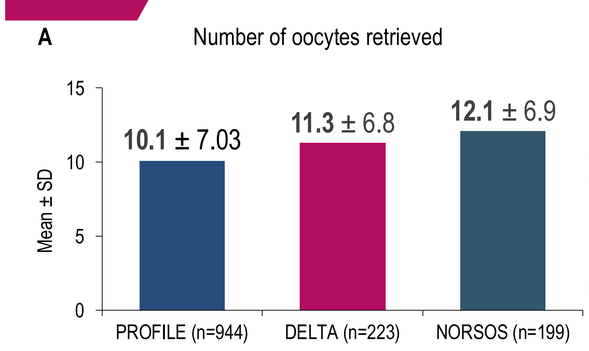
Table 1 Demographics and Baseline Characteristics (Full Analysis Set [FAS])

	PROFILE (n=944)	DELTA (n=223)	NORSOS (n=199)
Age, years	33.5 ± 4.7	33.0 ± 4.4	32.0 ± 4.0
<35 years	534 (56.6)	144 (64.6)	147 (73.9)
35–37 years	196 (20.8)	35 (15.7)	31 (15.6)
38–40 years	149 (15.8)	37 (16.6)	18 (9.0)
>40 years	65 (6.9)	7 (3.1)	3 (1.5)
Bodyweight, kg	67.1 ± 13.6	65.7 ± 11.8	68.9 ± 11.6
Primary reason for infertility			
Male factor	411 (43.5)	110 (49.3)	88 (44.2)
Unexplained infertility	227 (24.0)	41 (18.4)	71 (35.7)
Tubal infertility	134 (14.2)	42 (18.8)	11 (5.5)
Anovulatory infertility†	89 (9.4)	43 (19.3)	10 (5.0)
Other	284 (30.1)	62 (27.8)	19 (9.5)
Primary infertility	671 (71.1)	161 (72.2)	136 (68.7)
Duration of infertility, months	2.7 ± 2.1	3.4 ±2.2	2.4 ± 1.6
AMH, pmol/L (ng/mL‡)	20.3 ± 16.1 (2.84 ± 2.25) n=911	22.9 ± 18.6 (3.2 ± 2.6) n=222	21.3 ± 12.5 (2.98 ± 1.75)

Data are n (%) or mean ± standard deviation, *Participants could present with more than one reason for infertility in PROFILE and DELTA whereas the primary reason for infertility was recorded in the NORSOS study. †WHO anovulatory infertility groups I and II. ‡Conversion factor: AMH 7.1429 pmol/L equals 1.0 ng/mL.

The participants of these real-word studies had a higher dispersion for age and bodyweight than RCTs[1-4] for follitropin delta and included anovulatory PCOS patients

Figure 1 Ovarian Responses (FAS)



*Category for oocytes retrieved is <8 oocytes for the NORSOS study.

- **In clinical practice algorithmically dosed follitropin delta yielded on average ~10–12 oocytes**
- **The most common ovarian response category was 8–14 oocytes as per the dosing algorithm goal, confirming real-world performance of the follitropin delta dosing algorithm**

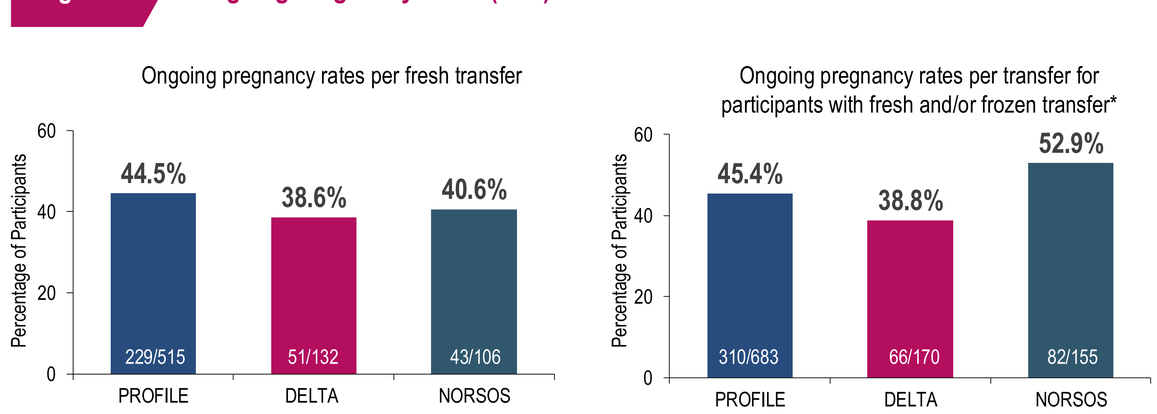
Table 2 Exposure, Ovarian Stimulation Protocol, Oocyte Retrieval and Embryo Transfer (FAS)

	PROFILE (n=944)	DELTA (n=223)	NORSOS (n=199)
Duration of treatment, days	10.4 ± 2.72	10.8 ± 5.2	9.9 ± 1.7
Total dose, µg	104.0 ± 35.01	122.2 ± 80.0	101.2 ± 31.0
Algorithmically calculated starting dose*	892 (94.5)	197 (88.3)	169 (84.9)
Dose adjustments during stimulation	57 (6.0)	40 (17.9)	12 (6.0)
GnRH antagonist protocol to prevent LH surge	848 (89.8)	196 (90.3)	171/193 (88.6)
Trigger for final follicular maturation			
hCG	764 (80.1)†	182 (81.3)	148 (74.4)‡
GnRH agonist	159 (16.8)†	41 (18.3)	30 (15.1)‡
Cycle cancellation prior to oocyte retrieval	55 (5.8)	12 (5.4)	5 (2.5)
Poor ovarian response	32 (3.5)	6 (2.7)	2 (1.0)
Excessive ovarian response	3 (0.3)	1 (0.4)	0
Other	20 (2.1)	5 (2.2)	3 (1.5)
Participants with oocyte retrieval	885 (93.8)	206 (93.2)	194 (97.5)
Participants with first embryo transfer (fresh or frozen)	775 (82.1)	170 (76.9)	155 (77.9)

Data are mean ± standard deviation or n (%).
*Follitropin delta dose determined by bodyweight and serum anti-Müllerian hormone level.
†In PROFILE, 30 participants received both hCG and GnRH agonist (included in both groups in the table), and 50 participants received no trigger.
‡In NORSOS, 12 participants received both hCG and GnRH agonist (included in both groups in the table) and 33 participants had missing data or did not receive a trigger.

Most participants received a gonadotropin-releasing hormone (GnRH) antagonist protocol and a human choriogonadotropin (hCG) trigger

Figure 2 Ongoing Pregnancy Rates (FAS)



*Includes women with more than one transfer (fresh or frozen), including a frozen transfer after an initial fresh transfer (only the latest transfer was considered).

In routine clinical practice, one ovarian stimulation cycle with algorithmic follitropin dosing resulted in ongoing pregnancy rates of ~38–45% per fresh cycle, similar to RCTs[1-4]

Table 3 Ovarian Hyperstimulation Syndrome Summary and Preventive Interventions (Safety Set)

	PROFILE (n=944)	DELTA (n=223)	NORSOS (n=199)
OHSS (any)	37 (3.9)	5 (2.2)	8 (4.0)*
Early OHSS (onset ≤9 days after triggering)	37 (3.9)	Not recorded	6 (3.0)
Moderate/severe intensity	7 (0.7)	1 (0.4)	0
Preventive interventions for early OHSS†	156 (16.5)	33 (14.8)	58 (29.1)
Embryo transfer cancellation	0	1 (0.4)	53 (26.6)
Coasting	8 (0.8)	4 (1.8)	0
GnRH agonist trigger with a fresh transfer	0	1 (0.4)	4 (2.0)
GnRH agonist trigger with 'freeze-all' strategy	107 (11.3)	24 (10.8)	44 (22.1)
Dopamine agonist	10 (1.1)	0	2 (1.0)

Data are n (%).
*All cases of OHSS were mild severity in the NORSOS study.
†Participants may have received more than one preventive intervention for early OHSS.

- **Overall rates of OHSS with algorithmic follitropin delta dosing in RWE studies were low (~2–4%), despite broader patient heterogeneity, and are consistent with RCT data[1-4]**
- **Clinicians were free to implement their own clinical approach on preventive interventions**

Abbreviations

AFC, antral follicle count; **AMH**, anti-Müllerian hormone; **CI**, confidence interval; **FAS**; full analysis set; **GnRH**, gonadotropin-releasing hormone; **hCG**, human choriogonadotropin; **IU**, international units; **ICSI**, intracytoplasmic sperm injection; **IVF,** in vitro fertilisation; **PCOS**, polycystic ovary syndrome; **OHSS**, ovarian hyperstimulation syndrome; **RCT**, randomised controlled trial; **RWE**, real-world evidence; **SD**, standard deviation.

References

1. Nyboe Andersen A, Nelson SM et al *Fertil Steril* 2017;107:387-396.
2. Qiao J et al *Hum Reprod* 2021;36:2452-2462.
3. Ishihara O et al *Reprod Biomed Online* 2021;42: 909-918.
4. Lobo R et al Hum Reprod 2024;39:1481-94.
5. Blockeel C et al Front Endocrinol 2022;13:992677.
6. Porcu-Buisson G et al Euro J Obstet Gyn 2024;293:21-26.
7. Pinborg A et al *Front Endocrinol* 2025;16:1613680.

Disclosures

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Contact information

For questions and comments, contact Enrica Gravotta at enrica.gravotta@ferring.com.