

337 Ovarian Responses and Pregnancy Rates with either Follitropin Delta 15 µg or Follitropin Alfa 225 IU starting doses: ADAPT-1 trial subgroup analysis by serum Anti-Müllerian Hormone (AMH) stratum (<15 or ≥15 pmol/L)

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OBJECTIVE

To evaluate ovarian responses and pregnancy outcomes to support clinical comparability between follitropin delta 15 µg and follitropin alfa 225 IU across AMH strata

KEY TAKEAWAYS

1 Ovarian responses and pregnancy rates were similar between follitropin delta 15 µg and follitropin alfa 225 IU treatment groups across AMH strata, supporting clinical comparability

2 In suitably selected patients, a starting dose of follitropin delta 15 µg/day results in good average oocyte yields and clinical pregnancy rates without increasing OHSS risk

3 Clinical comparability of follitropin delta 15 µg ≈ follitropin alfa 225 IU enables informed application of the µg dosing unit in clinical practice

BACKGROUND

- Ovarian stimulation with follitropin delta 10 µg/day provides a similar ovarian response to follitropin alfa 150 IU/day for serum concentration with a similar oocyte yield.¹ Using these results, the dose of follitropin delta 15 µg can be extrapolated to be comparable to follitropin alfa 225 IU
- Clinical trial data showed that conventionally dosed follitropin delta 15 µg/day and follitropin alfa 225 IU/day treatment groups have similar ovarian responses and clinical pregnancy rates, supporting clinical comparability for these starting doses, with low rates of early OHSS in selected patients suitable for higher gonadotropin starting dose²

METHODS

- Between 01-AUG-2022 and 16-APR-2024, participants, 18-40 years, undergoing IVF/ICSI and with no contraindications for a starting gonadotropin dose of 225 IU-per-day, were enrolled in Austria, France, Italy, Spain, and United Kingdom and randomised (2:1) to follitropin delta 15 µg-per-day or follitropin alfa 225 IU-per-day starting dose in a GnRH antagonist protocol
- In this subanalysis, endpoints were assessed by serum AMH subgroup: <15 or ≥15 pmol/L
- The primary endpoint was the number of oocytes retrieved, adjusted using a negative binomial model with treatment and serum AMH as factors. Clinical pregnancies from the first fresh/frozen transfer within 3 months of starting stimulation, adjusted using a logistic regression model with treatment and age group as factors, and OHSS rates were assessed

RESULTS

Table 1 ADAPT-1 Trial: Demographics and Baseline Characteristics by AMH Stratum (FAS*)

	Serum AMH <15 pmol/L		Serum AMH ≥15 pmol/L	
	Follitropin delta starting dose 15 µg / day, N=112	Follitropin alfa starting dose 225 IU / day, N=59	Follitropin delta starting dose 15 µg / day, N=85	Follitropin alfa starting dose 225 IU / day, N=37
Age, years	34.9 ± 3.6	34.4 ± 3.8	34.1 ± 4.0	34.7 ± 2.8
<35 years	43 (38.4)	24 (40.7)	37 (43.5)	18 (48.6)
Bodyweight, kg	65.1 ± 11.8	67.6 ± 11.1	68.1 ± 14.4	67.1 ± 10.4
BMI, kg/m ²	24.2 ± 4.18	24.9 ± 4.08	25.2 ± 5.14	24.4 ± 3.43
Primary reason for infertility				
Unexplained infertility	52 (46.4)	19 (32.2)	30 (35.3)	14 (37.8)
Mild/moderate male factor	31 (17.7)	20 (33.9)	26 (30.6)	7 (18.9)
Tubal infertility	14 (12.5)	9 (15.3)	9 (10.6)	4 (10.8)
Severe male factor	10 (8.9)	9 (15.3)	16 (18.8)	10 (27.0)
Endometriosis stage I/II	5 (4.5)	2 (3.4)	4 (4.7)	2 (5.4)
Primary infertility	71 (63.4)	32 (54.2)	60 (70.6)	25 (67.6)
Duration of infertility, months	34.2 ± 27.9	34.7 ± 24.2	40.5 ± 29.6	34.6 ± 18.3
AFC	10.9 ± 4.2	11.2 ± 4.3	16.3 ± 5.4	17.9 ± 6.1
Participants with previous IVF/ICSI cycle	43 (38.4)	21 (35.6)	30 (35.3)	12 (32.4)
Endocrine parameters Day 1 of stimulation				
AMH, pmol/L	9.2 ± 3.2	9.0 ± 3.1	21.6 ± 5.9	25.1 ± 11.8
Oestradiol, pmol/L	139.0 [106.0;187.0]	125.0 [106.0;169.0]	134.0 [106.0;168.5]	117.0 [99.0;169.0]
Progesterone, nmol/L	0.6 [0.6;1.0]	0.6 [0.3;1.3]	0.6 [0.6;1.3]	1.0 [0.6;1.0]

Data are mean ± standard deviation, median [interquartile range] or n (%).

*The full analysis set was identical to the intention-to-treat analysis set; however, there were seven participants who had missing serum AMH data and are not included in this analysis (follitropin delta group, n=4; follitropin alfa group, n=3). AMH was measured on Day 1 of stimulation with follitropin delta or follitropin alfa.

- Demographics were generally similar for the AMH subgroups; however, there were differences in mean antral follicle count and primary reason for infertility between AMH subgroups
- Clinical characteristics were generally similar between treatment groups for each AMH subgroup

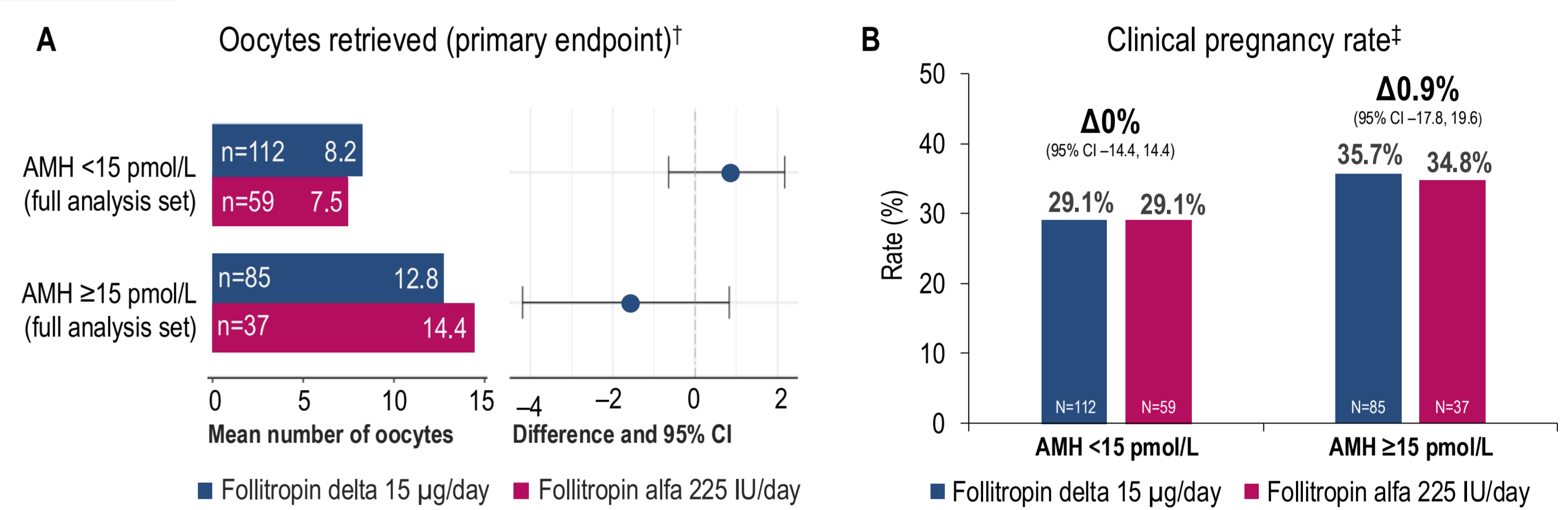
Disclosures

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Abbreviations

AFC, antral follicle count; AMH, anti-Müllerian hormone; ANOVA, analysis of variance; CI, confidence interval; FAS, full analysis set; GnRH, gonadotropin-releasing hormone; IU, international units; ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilisation; LS, least square; OHSS, ovarian hyperstimulation syndrome.

Figure 1 Number of Oocytes Retrieved and Clinical Pregnancy Rates by AMH Stratum (FAS*)



*The full analysis set was identical to the intention-to-treat analysis set; however, there were seven participants who had missing serum AMH data and are not included in this analysis (follitropin delta group, n=4; follitropin alfa group, n=3). Serum AMH was measured on Day 1 of stimulation with follitropin delta or follitropin alfa.
†Mean number of oocytes retrieved was estimated using a negative binomial regression model with treatment and serum AMH at stimulation Day 1 as factors.
‡Clinical pregnancy rates were estimated by AMH subgroups using a logistic regression model with treatment and age group as factors. Differences and confidence intervals were derived using the delta method.

- Ovarian responses and pregnancy rates were similar between treatment groups and were consistent across AMH strata, supporting the robustness of dose comparability between follitropin delta 15 µg and follitropin alfa 225 IU

Table 2 Gonadotrophin Dosing, Endocrine Parameters, Triggering of Final Follicular Maturation and Implantation Rates (FAS*)

	Serum AMH <15 pmol/L		Serum AMH ≥15 pmol/L		
	Follitropin delta starting dose 15 µg / day, N=112	Follitropin alfa starting dose 225 IU / day, N=59	Follitropin delta starting dose 15 µg / day, N=85	Follitropin alfa starting dose 225 IU / day, N=37	
Duration of treatment, days	9.2 ± 1.8	9.0 ± 1.4	9.1 ± 1.6	9.1 ± 1.0	
Total dose, µg [IU]	145.4 ± 36.5	155.7 ± 25.4 [2123 ± 346]	141.1 ± 29.7	152.2 ± 18.7 [2076 ± 255]	
Endocrine parameters at end of stimulation	Oestradiol, pmol/L	5043.0 [3226.0; 7311.0]	4940.0 [3149.0; 7487.0]	7494.5 [4635.5; 10901.5]	8122.0 [5839.0; 11483.0]
	Progesterone, nmol/L	2.9 [1.6; 3.5]	2.2 [1.6; 3.2]	2.9 [1.8; 4.3]	2.9 [1.9; 3.8]
Triggering of final follicular maturation	hCG	91 (81.3)	48 (81.4)	58 (68.2)	23 (62.2)
	GnRH agonist	21 (18.8)	8 (13.6)	27 (31.8)	14 (37.8)
	None	0	3 (5.1)	0	0

Data are summary statistics: n (%) or median [interquartile range].

*The FAS comprised all participants who received the study drug and was identical to the intention-to-treat analysis set; however, there were seven participants who had missing serum AMH data and are not included in this analysis (follitropin delta group, n=4; follitropin alfa group, n=3). Serum AMH was measured on Day 1 of stimulation with follitropin delta or follitropin alfa.

- Endocrine parameters on Day 1 of stimulation were similar across AMH strata but the ≥15 pmol/L subgroup had higher average serum oestradiol levels at end of stimulation compared with the 15 pmol/L subgroup

Table 3 Ovarian Hyperstimulation Syndrome Summary (Safety Analysis Set*)

	Serum AMH <15 pmol/L		Serum AMH ≥15 pmol/L	
	Follitropin delta starting dose 15 µg / day, N=112	Follitropin alfa starting dose 225 IU / day, N=59	Follitropin delta starting dose 15 µg / day, N=85	Follitropin alfa starting dose 225 IU / day, N=37
OHSS (any grade)†	2 (1.8)	1 (1.7)	5 (5.9)	2 (5.4)
Moderate/severe (Grades 3–5)	0	0	3 (3.5)	1 (2.7)
Early OHSS (onset ≤9 days after triggering; any grade)	2 (1.8)	1 (1.7)	3 (3.5)	2 (5.4)
Moderate/severe (Grades 3–5)	0	0	1 (1.2)	1 (2.7)
Any preventive interventions for potential early OHSS	8 (7.1)	4 (6.8)	21 (24.7)	10 (27.0)

Data are summary statistics: n (%).

*The safety set comprised all participants who received the study drug and was identical to the intention-to-treat analysis set; however, there were seven participants who had missing serum AMH data and are not included in this analysis (follitropin delta group, n=4; follitropin alfa group, n=3). Serum AMH was measured on Day 1 of stimulation with follitropin delta or follitropin alfa.

†OHSS was graded according to Golan et al.³

- Rates of OHSS and preventive interventions for potential early OHSS were comparable between trial drugs when assessed by AMH subgroup

References

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