# Cost-effectiveness of Follitropin Delta versus Follitropin Alfa in controlled ovarian stimulation for IVF/ICSI cycles in China

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## INTRODUCTION

In recent years, the prevalence of infertility in China has been on a continual upward trajectory. According to a report published in The Lancet RMNCAH Commission in China, the incidence of infertility in China has increased from 12% prior to 2007 to 18% by 2020.[1] Assisted reproductive technologies (ART) are recognized as one of the most efficacious treatments for infertility. Recombinant follicle-stimulating hormone (rFSH) is used in controlled ovarian stimulation (COS) for women pursuing in vitro fertilisation/intracytoplasmic sperm injection (IVF/ICSI) treatment.

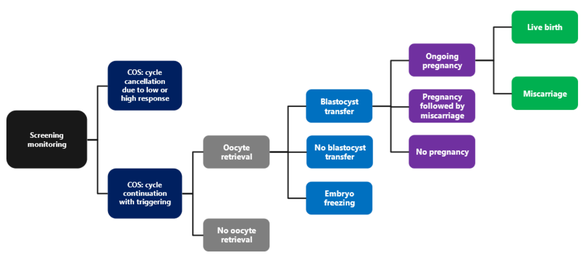
REKOVELLE (follitropin delta for injection) is the newest generation of recombinant-FSH (rFSH) approved by Chinese authorities (NMPA National Medical Products Administration) in April 2024. It offers a personalized dosing regimen based on patient's ovarian reserve profile (using anti-Müllerian hormone (AMH) levels) and body weight, achieving consistent daily dosing while maintaining efficacy in comparison with other follitropins.[2,3] The clinical safety and efficacy of follitropin delta was demonstrated compared with follitropins alfa and beta in three non-inferiority clinical trials (GRAPE, ESTHER & STORK studies).[4-6] The GRAPE study assessed the efficacy and safety of follitropin delta versus follitropin alfa in an Asian population including mainly Chinese patients. It is a randomised, controlled, multi-centre, assessor-blind trial conducted in 1,009 Asian patients from mainland China, South Korea, Vietnam and Taiwan, undergoing their first IVF/ICSI cycle. Randomisation was stratified by age (<35, 35-37, 38-40 years). The primary endpoint was ongoing pregnancy rate assessed 10-11 weeks after embryo transfer in the fresh cycle (non-inferiority limit -10.0%; analysis adjusted for age stratum).[4] This study further evaluates the cost-effectiveness of individualised dosed follitropin delta compared with follitropin alfa in women undergoing COS for IVF in China.

## METHODS

A decision-tree model (Figure 1) was developed comparing the outcomes of treatment with follitropin delta *versus* follitropin alfa through ongoing pregnancy (OP) and live birth (LB), using data from the pivotal clinical trial GRAPE (Pan-Asia). Follitropin alfa was dosed according to its license with a starting dose of 150 IU.

Women enter the model and begin COS. Depending on the response to follitropin treatment, they continue the process with oocyte retrieval and fertilisation by in vitro fertilization (IVF) and/or intracytoplasmic sperm injection (ICSI). Following blastocyst transfer women may have a clinical pregnancy leading to an OP or premature miscarriage. Finally, OP leads to LB or late miscarriage.

*Figure 1. Model structure*




The analysis was stratified by age (<35 years-old; 35-37 years-old; >37 years-old) and ovarian reserve profile (AMH level: <15 pmol/L; ≥15 pmol/L) and reflected a fresh single COS cycle. Early OHSS (appearing ≤9 after triggering) were modelled according to their severity (mild, moderate or severe). Costs were based on Chinese prices (taxes included) and the PHARMCUBE study and were estimated from the healthcare perspective in China. The PHARMCUBE study is a retrospective real-world evidence study with the objective to collect and estimate the healthcare resource use and costs of each step of typical Chinese IVF/ICSI processes, involving twenty private and public hospitals from seven regions in China. Acquisition cost of follitropins was estimated allowing for different available dosages and wastage, in ¥ (Chinese Yuan (CNY)). Uncertainty was assessed through deterministic and probabilistic sensitivity analyses (DSA and PSA). A thousand model iterations were performed in the PSA.

## RESULTS

Follitropin delta achieved numerically higher rates of OP (31.3%) and LB (31.3%) compared with follitropin alfa (OP: 25.9% [diff 5.4%, 95% CI: -0.2% ; 11.0%] and LB: 24.7% [diff 6.6%, 95% CI: 0.9% ; 11.9%]). Additionally, treatment with follitropin delta was associated with fewer miscarriages (4.8% vs. 6.3%) and lower incidences of OHSS (4.0% vs. 6.6%) than follitropin alfa (Figure 2).

As follitropin delta is based on personalised dosing regimens that depend on the patient's ovarian reserve and body weight, the average total dose of follitropin delta (78 µg) was lower than the average dose of follitropin alfa (110 µg). This difference led to lower treatment costs with follitropin delta compared with follitropin alfa (Table 1). In addition, follitropin delta achieved fewer miscarriages, fewer embryos frozen, and less OHSS than follitropin alfa, which also lead to lower cost. Thus, total treatment cycle cost with/without delivery was respectively ¥25,214 / ¥27,189 for follitropin alfa and ¥23,255 / ¥25,689 for follitropin delta (Table 1). These results lead to follitropin delta being the dominant treatment option (more efficient, lower costs) versus follitropin alfa (Figure 3).

*Figure 2. Health outcomes rates with follitropin delta or follitropin alfa, per patient*

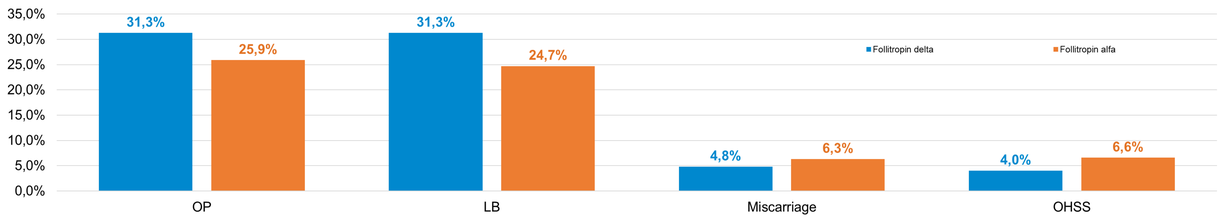
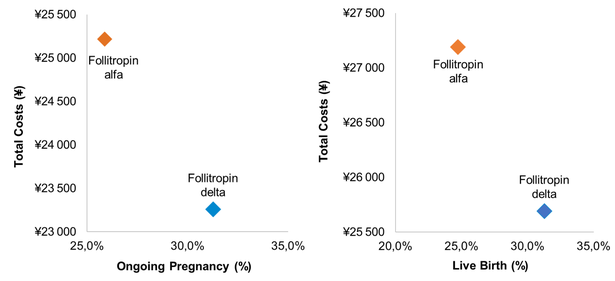



*Table 1. Disaggregated costs until LB and OP with follitropin delta or follitropin alfa, per patient*

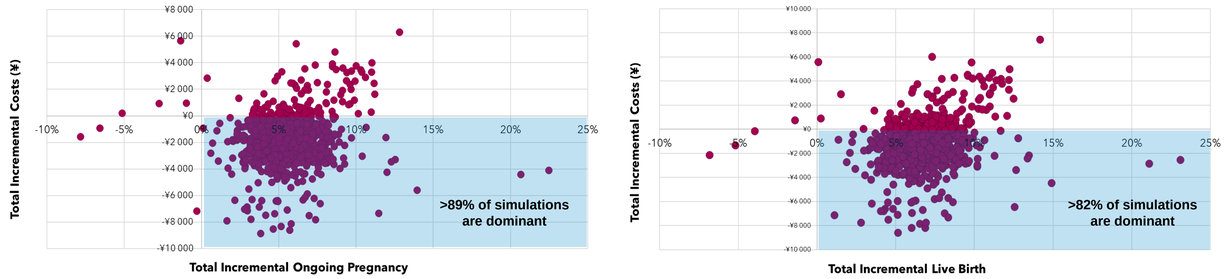
| Costs | Follitropin delta | Follitropin alfa |
|---|---|---|
| Acquisition of follitropins | ¥ 4,112 | ¥ 4,951 |
| COS and ART | ¥ 18,369 | ¥ 19,470 |
| OHSS management | ¥ 92 | ¥ 147 |
| Pregnancy until OP | ¥ 682 | ¥ 646 |
| Pregnancy until LB | ¥ 3,116 | ¥ 2,621 |
| **Total without delivery** | **¥ 23,255** | **¥ 25,214** |
| **Total with delivery** | **¥ 25,689** | **¥ 27,189** |

*Figure 3. Cost-effectiveness plane – Costs per OP or LB with follitropin delta or follitropin alfa*




Results of univariate DSA showed that IVF/ICSI's success rate, transition probabilities between different health states and the cost of pregnancy were the parameters with the higher impact on the results, while the PSA showed >89% probability of follitropin delta being dominant when assessing cost per OP, and >82% when assessing cost per LB (Figure 4).

*Figure 4. Cost-effectiveness plane – PSA results – ICER follitropin delta versus follitropin alfa*




## CONCLUSIONS

**Follitropin delta is cost-effective compared with follitropin alfa in ART for women undergoing COS protocols from Chinese health care perspective. This is attributed to better OP and LB rates, lower drug dose, less OHSS and** fewer embryos frozen**.**

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