A cost minimization analysis of gonadotropins for in vitro fertilization ovarian stimulation on oocyte- and embryo-based endpoints

N. Sumathi, D. Ezcurra, A. Cespedes, A. Xenakis, R. Beckerman

1EMD Serono, Inc.,* Rockland, MA, USA; 2CBPartners, New York, NY, USA

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Introduction

- Advancements in in vitro fertilization (IVF) have had positive effects in combating infertility, a global disease affecting 70–80 million reproductive-age women.
- The introduction of controlled ovarian stimulation (COS) for the induction of multi-follicular development, as well as treatment with gonadotropin-releasing hormone agonists down-regulation protocols, are techniques that have contributed greatly to the success rate of IVF.
- While a multitude of downstream factors in the IVF protocol of ovarian stimulation can affect live birth outcomes, gonadotropins are used in IVF treatment to stimulate the follicles for oocyte retrieval. Hence, when measuring the cost-effectiveness of gonadotropins, the number of oocytes retrieved is a meaningful endpoint because oocyte production is the first step in the IVF pathway that is most directly influenced by ovarian stimulation with these agents.
- Along these lines, it has been shown that the retrieval of 15 oocytes from one COS cycle correlates with an optimal chance per live birth.
- The number of embryos generated is also an important endpoint when considering gonadotropin cost-effectiveness, as the number of embryos generated has a direct influence on the number of embryos available for fresh or frozen/thawed transfers per COS, which directly affects the cumulative pregnancy and live birth rate.
- Accordingly, in determining the cost-effectiveness of gonadotropins agents used in IVF, it is important to consider outcomes resulting from treatment, and not merely focus on the drug cost per cycle.

Objective

- The purpose of this analysis was to quantify the cost-effectiveness of recombinant follicle stimulating hormone (r-hFSH) and highly purified human menopausal gonadotropin (HP-hMG) in the IVF process using Swedish cost inputs.
- The cost-effectiveness metrics analyzed were cost per oocyte retrieved, cost per embryo generated and the cost per optimal chance of live birth.

Methods

- An Economic-based model was developed to calculate the cost-effectiveness of COS with r-hFSH vs. HP-hMG utilisation in Sweden as measured by the cost per oocyte retrieved, cost per embryo generation and the cost per optimal chance of live birth for r-hFSH and HP-hMG.
- Costs per oocyte retrieved and embryo generated were calculated by multiplying the prices (ex-factory price) of r-hFSH and HP-hMG in Sweden by the average dose of gonadotropin utilised per COS cycle, divided by the average number of oocytes retrieved or embryos produced from the clinical trial.
- The cost per optimal chance of live birth was calculated by determining the cost of drug necessary to produce 15 oocytes, which has been shown in the literature to correlate with the greatest probability of obtaining a live birth.
- The model takes a payer and/or funder perspective and does not take into account societal costs.

Clinical data inputs

- A literature search was conducted in PubMed to identify prospective, randomized, head-to-head clinical trials comparing r-hFSH to HP-hMG on the endpoints of oocytes retrieved and embryos generated.
- Only studies that exclusively utilize GONAL-f as the r-hFSH were included; one article in the published literature satisfied this requirement, from which the inputs for oocytes retrieved, embryos generated.
- Clinical inputs for the model were inputted as the average values for those found in the published literature article (Table 1).

Cost of gonadotropin inputs in the model

- Only gonadotropin drug costs were included in the model, as medical costs of IVF were societal costs.
- Costs, which directly affects the cumulative pregnancy and live birth rate, were calculated for HP-hMG and GONAL-f.
- The cost per optimal chance of live birth for r-hFSH (8490 kr) was 17% less than for HP-hMG (10221 kr) in Sweden (Figure 1).
- The cost per oocyte retrieved for r-hFSH (566 kr) was 17% less than for HP-hMG (681 kr) in Sweden (Table 2).
- The cost per embryo generated for r-hFSH (2997 kr) was 11.8% less than for HP-hMG (3362 kr) in Sweden (Table 2).

Results

- The cost per optimal chance of live birth for r-hFSH (8490 kr) was 17% less than for HP-hMG (10221 kr) in Sweden (Table 2; Figure 1).
- The cost per embryo generated for r-hFSH (566 kr) was 17% less than for HP-hMG (681 kr) in Sweden (Table 2; Figure 1).
- The cost per optimal chance of live birth for r-hFSH (2997 kr) was 11.8% less than for HP-hMG (3362 kr) in Sweden (Table 2; Figure 1).

Conclusions

- Findings indicate that when measuring cost-effectiveness using cost per oocyte retrieved, cost per embryo generated and the cost per optimal chance of live birth, COS with mFSH is more cost-effective than COS with HP-hMG.
- Limitations of the analysis include the following:
  - The model outputs are cohort agnostic and did not take into consideration age, previous birth status, adverse events experienced, or other differentiating factors.
  - The model does not take into consideration the impact of different down-regulation protocol procedures.
  - The model assumes that there is a linear relationship between IU of gonadotropin used and oocytes retrieved, as well as embryos generated.
  - The model assumes that all patients treated with a given number of IUs achieved the same outcome in terms of oocytes retrieved and embryos generated (mean point estimate of respective dataset).
  - The model clinical inputs do not distinguish between r-hFSH and r-hMG in intra-cytoplasmic sperm injection techniques.

References

5. Emd Serono, Inc.* (*A subsidiary of Merck KGaA, Darmstadt, Germany.
6. KB Partners, New York, NY, USA

Disclosures

This study was supported by EMD Serono, Inc., Rockland, MA, USA; CBPartners, New York, NY, USA.

1. A subsidiary of Merck KGaA, Darmstadt, Germany.

Table 2: Model inputs.

<table>
<thead>
<tr>
<th>GONAL-f</th>
<th>HP-hMG</th>
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<tbody>
<tr>
<td>COST/OOCYTE RETRIEVED</td>
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</tr>
<tr>
<td>PRICE PER IU</td>
<td>EX-FAC TORY</td>
</tr>
<tr>
<td>23.0 kr</td>
<td>22.9 kr</td>
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<tr>
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<tr>
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</tr>
<tr>
<td>23.0 kr</td>
<td>22.9 kr</td>
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<tr>
<td>COST FOR OPTIMAL CHANCE OF LIVE BIRTH</td>
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<tr>
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<td>23.0 kr</td>
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Figure 1. Cost per oocyte retrieved.

Figure 2. Cost per embryo generated.

Figure 3. Cost per optimal chance of live birth.