A cost minimization analysis of gonadotropins for in vitro fertilization ovarian stimulation on pregnancy- and live birth–based endpoints in Germany

N. Sumathi,1 D. Ezcurra,1 A. Cespedes,1 A. Xenakis,2 R. Beckerman2

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

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Introduction

Ovarian stimulation in in vitro fertilization (IVF) has had positive effects in combating infertility, a global issue affecting 70 million reproductive-aged women.

The introduction of controlled ovarian stimulation (COS) for the induction of multiple follicular development, as well as treatment with gonadotropin-releasing hormone (GnRH) antagonists or down-regulation protocols, are techniques that have contributed greatly to the success rates of IVF.

When measuring the cost-effectiveness of gonadotropin preparations, 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.

This is particularly important since a multitude of downstream factors in the IVF protocol of ovarian stimulation can affect live birth outcomes. These factors include the method of collection, fertilization, embryo evaluation, embryo implantation, health of the mother, and ongoing and early pregnancy during pregnancy.

However, since many stakeholders are interested in understanding gonadotropin’s influence on “hander endpoints,” such as cost per pregnancy achieved and cost per live birth achieved, these were the specific endpoints central to this analysis.

Additionally, in determining the cost-effectiveness of gonadotropin agents used in IVF, it is important to consider outcomes resulting from treatment, and not merely focus on the drug cost per vial.

Objective

The purpose of this analysis was to quantify the cost-effectiveness of recombinant hFSH and uFSH-HP versus highly pure urinary follicle-stimulating hormone (uFSH-HP) in the IVF process of a hypothetical cohort.

The cost-effectiveness analysis methodology was cost per pregnancy achieved and cost per live birth achieved.

Methods

Model structure

An Excel-based model was built to estimate the drug cost per pregnancy and drug cost per live birth resulting from a hypothetical cohort of 1000 women undergoing IVF in Germany.

To mimic the IVF pathway within the model, the cohort of patients underwent one round of ovarian stimulation, where the mean number of embryos generated was assumed to be 5 or 1 to 11 embryos for r-hFSH and 3.5 to 4 embryos for uFSH-HP, depending on which database (Bissonnette or Bergh) was used.

Since all cycles were included in the database, the proportion of embryos that could be used for both fresh and frozen embryo transfer was not considered.

With every round of fresh or frozen embryo cycles there was an associated percent chance of achieving cumulative pregnancy birth as sourced from the literature (clinical trial data).

Model inputs

Clinical data inputs

A literature search was conducted in PubMed to identify prospective, randomised, head-to-head clinical trials comparing r-hFSH to uFSH-HP on the endpoint of embryos generated.

Only studies that exclusively utilized GnRH as the down-regulation protocol and included, in the published literature satisfied this requirement, from which the inputs, embryos generated and IUs used were sourced.

Cumulative pregnancy/embryo-pregnancy generated ratios incorporated into the model were sourced from a Canadian study on cumulative pregnancy rates from IVF.

Cumulative live birth/embryo-pregnancy generated rates were incorporated in the model by multiplying the cumulative pregnancy/embryo-pregnancy rates by the cumulative live birth/embryo-pregnancy rates sourced from the German FRYDMAN DATASET.

Clinical inputs for the model were dictated as the average values for those found in the published literature (Table 1, Table 2).

Table 1: Model inputs

<table>
<thead>
<tr>
<th>Dataset</th>
<th>r-hFSH</th>
<th>uFSH-HP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Pregnancy</td>
<td>4068 €</td>
<td>3446 €</td>
</tr>
<tr>
<td>Cost Per Pregnancy</td>
<td>1795 €</td>
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Results

Cost-effectiveness results

Comparison of r-hFSH resulted in a cost per pregnancy of 1795 € (Bissonnette et al.) and 1500 € (Ptykmann et al.) less than treatment with uFSH-HP (Table 1, Figure 2).

The cost per live birth was 349 € (Bissonnette et al.) and 200 € (Ptykmann et al.) less with r-hFSH than for uFSH-HP (Table 2, Figure 3).

Conclusions

Findings indicate that when measuring cost-effectiveness using cost per pregnancy or live birth achieved, COS with r-hFSH is more cost-effective than COS with uFSH-HP.

Limitations of this analysis:

The model outputs are cohort agnostic and did not take into consideration age, ovarian stimulation, where the mean number of embryos generated was assumed to be 5 or 1 to 11 embryos for r-hFSH and 3.5 to 4 embryos for uFSH-HP, respectively were selected; these embryos were then available for fresh and frozen embryo transfer.

However, since many stakeholders are interested in understanding gonadotropin’s influence on “hander endpoints,” such as cost per pregnancy achieved and cost per live birth achieved, these were the specific endpoints central to this analysis.

Additionally, in determining the cost-effectiveness of gonadotropin agents used in IVF, it is important to consider outcomes resulting from treatment, and not merely focus on the drug cost per vial.

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Limitations of this analysis:

The model outputs are cohort agnostic and did not take into consideration age, previous birth, adverse events experienced, or other differentiating factors.

The model does not differentiate between IVF and IVP = intracytoplasmic sperm injection techniques or between down-regulation protocol procedures.

It is assumed that the delivery rate is an approximate approximation of the live birth rate.

It is assumed that the pregnancy rate for SET and DET are equal.

All embryo inputs are of equal quality and are not voluntarily discarded within the procedure.

The model assumes mean point estimates from sourced data and that there is a linear relationship between IUs used and oocytes retrieved.

References

8. latency before ovum collection.
9. latency before ovum collection.
10. in women undergoing IVF in Germany.

Acknowledgments

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Disclosures

Dr. Ezcurre is employed by EMD Serono, Inc. Dr. Xenakis is employed by EMD Serono, Inc. Dr. Beckerman is a consultant to EMD Serono, Inc. The roles taken by these individuals did not influence the content of this manuscript, nor were the authors compensated in any way for their content development.

Figure 1

Figure 2

Figure 3

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<th>Cost Per Live Birth/Achieved</th>
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Figure 2: Cost per pregnancy achieved.

Figure 3: Cost per live birth achieved.

Figure 1: Model methodology to calculate cost per pregnancy and cost per live birth achieved.

Table: 1. Model inputs.

<table>
<thead>
<tr>
<th>COST FOR PREGNANCY/ACHIEVED</th>
<th>COST FOR LIVE BIRTH/ACHIEVED</th>
</tr>
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r-hFSH vs uFSH-HP