



Fostimon, a new generation human-derived FSH, in a clinical setting: evidence for improved efficacy and new opportunities of investigation

J.G. Grudzinskas

The London Bridge Fertility, Gynaecology and Genetics Centre, London Bridge, UK SE1 9RY

Fostimon is a new generation human-derived FSH product manufactured by IBSA, Switzerland. It is claimed by the manufacturer that this newly developed purification process leads to improved preservation of the original glycosylation of FSH resulting in with a product with a unique composition of FSH isoforms. The question is whether such differences do actually translate into any practical clinical advantages over existing products.

Fostimon has been extensively investigated in two company sponsored, large, multicentre studies aiming to assess its clinical efficacy and tolerability with respect to a reference recombinant FSH (rFSH) for regulatory purposes. These still to be published studies, one in Europe and one in the USA, involving a total of 297 cycles have shown complete therapeutic equivalence between the two products tested with overlapping results for all primary or secondary outcome variables assessed. Thus, there is a reliable bulk of evidence indicating that Fostimon is a suitable alternative to other FSH products even though studies were not designed to detect differences in quality or clinical outcome.

Nevertheless, these questions have been targeted and to some extent addressed by other independent studies. The very first question was whether the extended range of FSH isoforms would have resulted in better oocyte/embryo quality and was investigated by Selman et al. (*Fertil. & Steril.* 2002; 78(5): 1061-67). A total of 267 cycles were treated with either Fostimon or rFSH and all embryos were carefully graded. Similar to other studies, the standard clinical variables did not differ between the groups even though there was a trend in favour of Fostimon for clinical pregnancy rates (46.5% vs. 36.8%), implantation rates (22.1% vs. 15.8%) and total drug usage (51.7 vs. 60.5 vials). By contrast, the embryo grading resulted in a significant advantage for Fostimon in terms of top quality embryos (42.1% vs. 33.5%, $p < 0.05$).

Another study from Mohamed et al. (*Fertil. & Steril.* 2006; 85(5): 1398-1403) investigated the performance of Fostimon compared to rFSH in 241 stimulation cycles in women aged >40 years. Also in this study there were no differences in the main clinical outcome variables, however the efficiency of Fostimon was far higher than that of rFSH in terms of the lower total drug usage (3213 vs. 5533 IU, $p < 0.001$) and the lower amount of FSH IU per oocyte yield (608 vs. 1146 IU, $p < 0.01$). These results indicate a clear cut advantage in favour of the new FSH and support the speculative view about the benefits of with its composition namely, more glycosylated FSH, such as may be preferentially released by the pituitary gland in older women to overcome increasing ovarian resistance.

A more recent report from Selman et al. (*J. Assist. Repr. Gen.*, 2007 in press) has investigated the hypothesis that the highly glycosylated isoforms of Fostimon may have advantages in the recruitment phase, as suggested by the finding that in natural cycles such isoforms are preferentially released when the cohort of follicles start to grow, i.e. in the late luteal and early follicular phase. Thus, aiming to isolate the effects of Fostimon's isoforms in the recruitment phase, a fixed dose stimulation with rFSH was compared with a fixed dose sequential protocol in which Fostimon was administered during the initial 6 days and then replaced by rFSH until final maturation. In women in the sequential protocol group, almost double pregnancy rates (43.9% vs. 22.1%, $p < 0.001$) and implantation rates (27.5% vs. 13.2%, $p < 0.001$) were observed, indicating that the unique FSH isoforms of Fostimon might have led to improved recruitment.

In summary, Fostimon has not only been shown to have a clinical therapeutic profile comparable to rFSH, but also to have unique qualities, which may be due to a particular composition of FSH isoforms accounting for its practical clinical advantages. These data should stimulate further studies to confirm and expand current findings and to further explore the potential of this new therapeutic concept.