

## Lutropin Alfa

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Recombinant-DNA technology has provided us with qualitatively and quantitatively consistent preparations of gonadotropins. Thus, we can treat patients separately with recombinant human follicle stimulating hormone (r-hFSH) and recombinant human luteinizing hormone (r-hLH) according to the specific indication. Hypogonadotropic hypogonadism is the main indication where r-hLH is used along with r-hFSH. This clinical approach is consistent with the classical 'two cell-two gonadotropins' theory.

Recent studies have identified granulosa cells as additional targets for luteinizing hormone (LH), after the intermediate-late follicular phase.<sup>[1,2]</sup> This line of evidence led us to hypothesize that LH supplementation may also optimize follicular growth and steroidogenesis in normogonadotropic women undergoing pituitary desensitization and ovarian stimulation with r-hFSH. On this basis, protocols employing r-hLH have been tested in different subsets of patients undergoing *in vitro* fertilization (IVF). Initial clinical trials have suggested that patients aged >35 years and normogonadotropic women displaying ovarian resistance to exogenous FSH may benefit from the addition of r-hLH.<sup>[3-6]</sup>

Although these lines of evidence are based on randomized controlled trials, data regarding pregnancy rates in elderly patients were derived by 'a posteriori' stratification processes.<sup>[4,5]</sup> Furthermore, randomized controlled trials investigating the effects of r-hLH in women with suboptimal response to FSH were not based on power analysis<sup>[3]</sup> or evaluated the mean number of oocytes as the primary endpoint.<sup>[6]</sup>

In all the studies, normogonadotropic patients were given once-daily r-hLH 75–150 IU. These doses were established based on trials performed in women with hypogonadotropic hypogonadism and in which mono-ovulation represented the clinical target. Recombinant LH is characterized by a short half-life (1.9 h) and, unlike hCG, mediates a rapid and transient message. It is not possible to exclude the possibility that during multiple follicular growth, a higher and more persistent LH stimulus may be required.

In conclusion, there appears to be no doubt about the usefulness of r-hLH in hypogonadotropic hypogonadal women. Although initial data from normogonadotropic women undergoing IVF are encouraging, there is a lack of adequately sized studies evaluating implantation and pregnancy rates as primary endpoints. Moreover, higher dosages of r-hLH should be tested in these patients. ▲

## References

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