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Ganirelix

A Viewpoint by Thomas Strowitzki

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Ganirelix is 1 of 2 gonadotropin-releasing hormone (GnRH) antagonists now clinically available (the other is cetrorelix), which has been developed for the prevention of premature luteinising hormone (LH) surges in women undergoing controlled ovarian hyperstimulation in combination with assisted reproductive techniques (ART). The current standard protocol in ART cycles combines a prolonged ovarian suppression with GnRH agonists followed by ovarian stimulation with gonadotropins. GnRH agonists act via pituitary receptor downregulation after an initial release of gonadotropins from the pituitary gland (flare-up), resulting in pituitary desensitisation. In contrast, GnRH antagonists block GnRH receptors by competitive inhibition.

In a dose finding study in *in vitro* fertilisation (IVF) cycles only 1 of 69 patients who received a daily injection of ganirelix 0.25mg showed an LH rise during treatment.[1] No premature LH rise was reported in groups who received ganirelix at a daily dose of at least 0.5mg. The clinical pregnancy rates were acceptable in groups with a maximum daily dose of 0.5mg. The highest clinical pregnancy rate per embryo transfer was achieved with a daily injection of 0.25mg (40.3%). GnRH antagonists offer some important clinical advantages. They allow immediate suppression of LH and a shorter stimulation time when compared to the long agonist protocol, with lower gonadotrophin consumption and a lower risk of developing ovarian hyperstimulation syndrome (OHSS). Finally, ovulation can be induced by means of a GnRH agonist instead of human chorionic gonadotrophin, thus further reducing the risk of OHSS development. However, it has not been shown that antagonist protocols result in superior pregnancy rates compared to standard long protocols.

In summary, GnRH antagonists provide a clinically well established, short and convenient treatment option, particularly for patients at risk of developing OHSS or for patients with a poor response to a standard long protocol. In future studies, antagonists will be used for other gynaecological disorders where ovarian suppression might be useful, such as endometriosis or myoma of the uterus. ▲

References

1. Mannaerts B, Devroey P, Abyholm T, et al. A double-blind, randomized, dose-finding study to assess the efficacy of the gonadotrophin-releasing hormone antagonists ganirelix (Org 37462) to prevent premature luteinizing hormone surges in women undergoing ovarian stimulation with recombinant follicle stimulating hormone (Puregon). Hum Reprod 1998 Nov; 13: 3023-31