

A randomized, dose-finding trial to establish the ovarian response to a single injection of Org 36286 for sustained follicular stimulation

P. Devroey^{1,*}, N. Koper², B. Mannaerts²

¹Dutch-speaking Free University, Center of Reproductive Medicine, Brussels, Belgium; ²NV Organon, Global Development Department, Oss, The Netherlands

*On behalf of the Org 36286 dose-finding study group

Introduction: Org 36286 (corifollitropin alfa, NV Organon) is a new biological entity developed for patients undergoing fertility treatment. It is a recombinant gonadotropin molecule in which the FSH beta chain is fused with the carboxy-terminal peptide of the hCG beta subunit. Consequently, Org 36286 has a longer elimination half life. One single injection of Org 36286 induces sustained multiple follicular development during the first week in patients undergoing controlled ovarian stimulation (COS) for IVF/ICSI, followed by daily recombinant FSH up to the day of triggering ovulation.

Materials and methods: In this multicenter dose-finding trial, 233 subjects received a single SC injection of Org 36286 in doses of 60, 120 and 180mg on menstrual cycle day 2 or 3, followed by a fixed dose of 150 IU rFSH (Puregon_®, NV Organon) from stimulation day 8 onwards. The primary objective was to determine a positive dose–response curve for the number of cumulus-oocyte complexes.

A fixed dose regimen of daily 150 IU Puregon_® was applied as a reference (82 subjects).

Results: Serum Org 36286 concentrations vs. time were described by a one-compartment

pharmacokinetic model with first-order absorption, first-order elimination, and body weight as covariate. The mean elimination half-life ($t_{1/2}$) was 66 h and the mean estimated time-to-peak concentration (T_{max}) was 42 h. Pharmacokinetics of Org 36286 was dose proportional. The number of follicles, serum E2 and inhibin B levels increased with the dose of Org 36286. Accordingly, a statistically significant dose response ($p < 0.0001$) was found for the mean number of cumulus-oocyte complexes retrieved, as 5.2, 10.3 and 12.5 oocytes were retrieved in the 60, 120 and 180mg Org 36286 group, respectively. In the Puregon_® group, a mean of 7.7 oocytes was retrieved. The main reason for cancellation was insufficient ovarian response, occurring in 31.2, 2.6 and 3.8% of the subjects in the 60, 120, and 180mg Org 36286 groups, respectively, and 7.3% of the subjects in the Puregon_® group. OHSS was reported as a serious adverse event six times, i.e. twice each in the 120mg group, the 180mg group and the Puregon_® group. Treatment with Org 36286 was well tolerated and non-immunogenic.

Conclusions: Org 36286 is the first compound in a new class of gonadotropins termed as sustained follicle stimulants. All three test doses of Org 36286 were able to induce multiple follicular growth; however, in view of the high cancellation rate, the lowest dose (60mg) Org 36286 was demonstrated to be insufficient

in the one-week regimen tested. Treatment with Org 36286 was safe and
Abstracts of the 22nd Annual Meeting of the ESHRE, Prague, Czech Republic,
18–21 June 2006

i68

well tolerated and potentially offers a promising regimen for patients undergoing
ovarian stimulation for IVF/ICSI.