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Single dose pharmacokinetics and effects on follicular growth and serum hormones of a long-acting recombinant FSH preparation (FSH-CTP) in healthy pituitary-suppressed females.

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BACKGROUND: A long-acting FSH preparation has been developed by site-directed mutagenesis and gene transfer techniques. **METHODS:** In this open-label trial, we investigated the pharmacokinetic and pharmacodynamic properties of FSH-CTP (corifollitropin alpha, Org 36286) in healthy female volunteers. Twenty-four subjects were treated with a high-dose oral contraceptive (OC) to suppress pituitary function. A single dose of 15, 30 or 60 micro g FSH-CTP was injected (s.c., eight subjects per dose group) and seven of these 24 subjects were subsequently treated with a single dose of 120 micro g. **RESULTS:** Maximum serum FSH-CTP concentrations (0.42, 0.66, 1.49 and 3.27 ng/ml after administration of 15, 30, 60 and 120 micro g Org 36286 respectively) were reached between 36 and 48 h after injection and $t(1/2)$ varied between 60 and 75 h. Dose proportionality was shown across the studied dose range, whereas $t(max)$ and $t(1/2)$ were dose independent. In most subjects follicular growth was observed; the number and maximum diameter of the follicles increased with the dose. Follicles with a diameter vertical line 8.0 mm were observed only in the 60 and 120 micro g dose groups, diameters between 12.0 and 15.9 mm occurred only in the 120 micro g group. Serum LH and 17beta-oestradiol levels remained low due to profound pituitary suppression whereas inhibin-B levels increased with dose. Maximum mean inhibin-B levels were 30.4, 322.7 and 1059.3 pg/ml in the 30, 60 and 120 micro g dose group respectively. The preparation was safe and well tolerated, and no FSH-CTP antibody formation was observed. **CONCLUSIONS:** The pharmacokinetics of FSH-CTP were shown to be proportional with the dose. The elimination half-life was approximately two times longer than that of rFSH. A single dose of FSH-CTP was shown to be safe and able to induce multiple follicular growth accompanied by a dose-dependent rise in serum inhibin-B concentrations.