The international Academy of Human Reproduction

17th World Congress of the Academy of Human Reproduction

15–18 March 2017

Rome, Italy

TITLE

PHARMACOKINETIC CHARACTERISTICS OF VARIOUS DOSES OF VAGINAL PROGESTERONE PESSARIES IN COMPARISON TO PROGESTERONE VAGINAL GEL

AUTHOR/S

Duijkers I (NL) [1], Klingmann I (BE) [2], Wargenau M (DE) [3], Prinz R (DE) [4], Hrafnsdottir S (IS) [5], Magnusdottir T B (IS) [6], Klipping C (NL) [7]

ABSTRACT

Context: The optimal dose and efficacy of progesterone vaginal pessaries have yet to be determined when used for luteal phase support in assisted reproduction

Objective: Assess and compare pharmacokinetics (PK) of progesterone vaginal pessaries to progesterone vaginal gel

Methods: Randomized Phase 1 study

Patients: 125 healthy female volunteers, 18-45 years old

Interventions: Progesterone vaginal pessaries (Cyclogest®) 100mg twice daily (BID), 200mg BID, 400mg daily (OD) or BID or progesterone vaginal gel 90mg (Crinone®) OD

Outcome Measure(s): PK parameters, assessed after first dose on Day 15 (single dose, SD) and last dose on Day 24 (multiple dose, MD). Parameters assessed: area under the concentration-time curve (AUC0-12h; AUC0-24h; AUC0-tlast,MD), maximum observed plasma concentration (Cmax,SD;Cmax,MD), time to Cmax (Tmax,SD;Tmax,MD) and terminal phase half-life (t1/2,MD).

Result(s): SD PK characteristics were comparable over the 12 hour sampling interval for 200 mg and 400 mg Cyclogest®. A dose-dependent effect on PK was observed only up to 200 mg after SD. The 100 mg Cyclogest® dose showed slightly larger AUC(0-12h) and Cmax,SD than 90 mg Crinone® but earlier Tmax,SD. After MD, mean plasma progesterone concentrations of Cyclogest® 400 mg BID, 400 mg OD and 200 mg BID consistently exceeded those of Crinone® during the 24 hours dosing interval. A dose-dependent but not dose-proportional effect on progesterone PK could clearly be observed after MD with Cyclogest®. Both Cmax,MD and AUC(0-24h) were at least doubled after administration of Cyclogest® 400 mg BID in comparison to Crinone. Both Cyclogest® and Crinone® were safe and well tolerated.

Conclusions: PK of progesterone vaginal pessaries showed a dose-dependent but not dose-proportional increase of plasma progesterone levels.

Funding: Actavis Group PTC ehf., Iceland, part of Teva Pharmaceuticals; LD Collins

INSTITUTE

[1] Dinox BV, [2] Pharmaplex bvba, [3] M.A.R.C.O. GmbH & Co. KG, [4] M.A.R.C.O. GmbH & Co. KG, [5] Actavis Group PTC ehf, [6] Actavis Group PTC ehf, [7] Dinox BV