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TITLE

PROGESTERONE FOR LUTEAL PHASE SUPPORT: SEARCHING FOR THE OPTIMAL DOSE

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ABSTRACT

Context: Progesterone vaginal pessaries are widely used off-label for luteal phase support in assisted reproduction cycles (ART). No clinical trials have been performed yet to determine the optimal dose and to prove the efficacy for this indication.

Objective: To determine which progesterone vaginal pessary dose regimen induces adequate secretory transformation of the endometrium in a pharmacodynamic model, in comparison with progesterone vaginal gel and placebo.

Methods: A phase I, randomized, observer-blind crossover study.

Patients: Healthy female volunteers 18-45 years old, 179 enrolled, 125 treated.

Interventions: Progesterone vaginal pessaries 100mg twice daily (bid), 200mg bid, 400mg daily (od) or bid; progesterone vaginal gel 90mg od or placebo bid.

Main Outcome Measures: Endometrial histology, single- and multiple-dose pharmacokinetics, safety and tolerability.

Results: Frequencies of secretory transformation of the endometrium, i.e. adequate responses, were comparable during treatment with 200 mg and 400 mg vaginal pessaries bid and 90 mg vaginal gel od, whereas lower secretory transformation rates were observed with 100 mg bid and 400 mg od. The late secretory state of the endometrium, which is considered most adequate, was observed slightly more often during treatment with 400 mg vaginal pessaries bid. Multiple-dose pharmacokinetics showed a dose-dependent, but not dose-proportional, increase of plasma progesterone levels. The lowest incidence of bleeding and spotting was reported with 400 mg vaginal pessaries bid.

Conclusions: The 400 mg bid vaginal pessary dose regimen seems to be optimal for luteal phase support and as effective as 90 mg vaginal gel od. The efficacy of this dose regimen will be confirmed by evaluating pregnancy rates in ART.

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INSTITUTE

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