# CLINICAL SUMMARY

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| **Title** | Oral dydrogesterone versus intravaginal micronized progesterone gel for luteal phase support in IVF: a randomized clinical trial |
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## Objective

Is oral dydrogesterone 30 mg daily non-inferior to 8% intravaginal micronized progesterone gel 90 mg daily for luteal phase support in *in vitro fertilization* (IVF)?

## Study Design

- Lotus II was a randomized, open-label, multicenter, phase III non-inferiority clinical study, performed across 37 sites in 10 countries.
- Patients were randomized to oral dydrogesterone (Duphaston®) 10 mg tablets three times daily or 8% intravaginal micronized progesterone gel 90 mg (Crinone®) once daily.
- In total, 1034 subjects were randomized to receive either oral dydrogesterone (n=520) or intravaginal micronized progesterone gel (n=514).
- Luteal phase support was started on the day of oocyte retrieval and continued until 12 weeks of gestation if a positive pregnancy test was obtained 2 weeks after embryo transfer and no miscarriage occurred.
- The primary outcome measure was the presence of fetal heartbeats at 12 weeks of gestation as determined by transvaginal ultrasound.

## Results

- In the oral dydrogesterone and intravaginal micronized progesterone gel groups, 494 and 489 subjects were included in the full analysis set (FAS).
- Pregnancy rates at 12 weeks of gestation for the oral dydrogesterone and intravaginal micronized progesterone gel groups were 38.7% and 35.0% in the FAS, respectively ((adjusted difference, 3.7%; 95% CI: −2.3 to 9.7). In both the FAS and per protocol sample (PPS), non-inferiority of oral dydrogesterone versus intravaginal micronized progesterone gel was demonstrated as the lower-bound CI was greater than the non-inferiority margin of -10%.
- Live birth rates in the FAS were 34.4% in the oral dydrogesterone group and 32.5% in the MVP group respectively (adjusted difference 1.9%; 95% CI: −4.0 to 7.8).
- Oral dydrogesterone was well-tolerated, and the incidence of treatment emergent adverse events for mothers and newborns was comparable to that of intravaginal micronized progesterone gel in this study. The proportions of subjects with at least one TEAE in the oral dydrogesterone and MVP gel groups were 53.1 and 48.6%, respectively. The proportion of fetuses/newborns with at least one TESAE was 12.7% in the oral dydrogesterone group and 11.4% in the MVP gel group.

## Conclusions

The present study confirms the findings of the Lotus I trial (Tournaye *et al.*, Hum Reprod. 2017), which already established oral dydrogesterone as a viable alternative to vaginally administered micronized progesterone due to its efficacy and comparable tolerability in the studies.