

# Evaluation of a New Sustained-Release Deslorelin Acetate for Induction of Ovulation in Mares

Edward L. Squires, MS, PhD\*; and Barry W. Simon, DVM

A deslorelin acetate suspension in a slow-release formulation<sup>a</sup> induced ovulation in 77% to 90% of cyclic mares within 48 hours after injection and did not alter interovulatory interval (21, 25 days, treated versus controls) or pregnancy rate. Authors' address: Gluck Equine Research Center, University of Kentucky, Lexington, KY 40546; e-mail: edward.squires@uky.edu. \*Corresponding author. © 2011 AAEP.

## 1. Introduction

Proper timing of breeding with ovulation is essential for maximizing pregnancy rates. The goal, whether using natural mating or insemination of cooled or frozen/thawed semen, is to breed the mare only once per cycle, close to ovulation. Several products are available to induce ovulation in mares including a GnRH agonist (deslorelin acetate) and human chorionic gonadotropin (hCG). Deslorelin is available as an implant<sup>b</sup> in some countries outside the United States and formerly a compounded product in the United States. However, studies have shown that some mares given deslorelin acetate implant<sup>b</sup> have an extended interovulatory interval.<sup>1</sup> HCG, although quite effective in inducing ovulation in most mares, is less effective in older mares and mares that have been given multiple doses in one breeding season.<sup>2</sup> A new product, deslorelin acetate suspended in sucrose acetate isobutyrate (SAIB)/propylene carbonate (70:30 WT: WT), has been approved by the FDA (NADA 141-139, 11/15/10) and is commercially available.<sup>a</sup> The objective of

the study was to (1) select the efficacious dose of deslorelin acetate for induction of ovulation and (2) determine the efficacy of the most effective dose in a multicentered clinical field trial.

## 2. Materials and Methods

In Part 1 of the first dose trial, 10 normal-cycling, nonlactating mares per group were assigned to a single intramuscular injection of 0, 0.45, 0.9, 1.35, or 1.8 mg deslorelin acetate once they had acquired a follicle of 30 to 40 mm in diameter during estrus. Mares were examined daily by palpation per rectum and ultrasonography for ovarian follicular development and ovulation. The percentage of mares ovulating in 48 hours was determined. In Part 2 of this study, mares were treated as above with either saline or 0.9 or 1.8 mg deslorelin acetate (20 mares per treatment group and 38 controls), and the number of mares ovulating in 48 hours was determined. A second study compared deslorelin acetate at a dose of 0, 0.9, 1.35, or 1.8 mg (12 mares/group).

Based on these dose-response studies, the dose of 1.8 mg deslorelin acetate was selected for use in a

---

## NOTES

multicentered efficacy trial. Locations included one location each in Australia and Ireland and four locations in the United States. Treatments with placebo (saline) or deslorelin acetate (1.8 mg) were blinded to the evaluator. A total of 191 mares (97 placebo and 94 deslorelin acetate) were treated (67% lactating, 10% maiden, 19% barren, and 4% unknown). A single injection of either 1 mL saline (placebo) or 1.0 mL sustained release deslorelin acetate<sup>a</sup> (1.8 mg deslorelin acetate) was given once mares had established a normal estrous cycle (previous ovulation and had returned to estrus) and had an ovarian follicle 30 to 40 mm in size, during estrus lasting for at least 2 days. Ovaries were examined daily by palpation per rectum and ultrasonography. The mares were inseminated or bred by natural cover. The percentage of mares ovulating within 48 hours and the percentage that became pregnant after treatment was determined. Pregnancy was determined by ultrasonography at 18 and 50 days after breeding. For the mares that did not become pregnant, interovulatory interval was calculated between successive cycles.

### 3. Results

The percentage of mares in Part 1 of Trial 1 ovulating in 48 hours was 20%, 30%, 90%, 80%, and 90%, respectively, for 0, 0.45, 0.9, 1.35, and 1.8 mg deslorelin acetate. In Part 2 of Trial 1, the percentage of mares ovulating in 48 hours was 20%, 70%, and 90% for 0, 0.9, and 1.8 mg deslorelin acetate treatment groups. In the second study, the percentage of mares ovulating in 48 hours was 6.3%, 70%, and 90% for mares given 0, 0.9, 1.8 mg deslorelin acetate.

In the multicenter trial, mares were given either saline or 1.8 mg deslorelin acetate. The proportion of nonpregnant mares ovulating within 48 hours of treatment during estrous cycles 1, 2, 3, and overall during the study was 24%, 36%, 33%, and 27% for controls and 72%, 83%, 92%, and 77% for treated mares. The mean interovulatory interval did not differ for sustained release deslorelin acetate<sup>a</sup>-treated mares (21 days) compared with controls (25 days). The percentage of interovulatory intervals greater than 29 days was 8% for sustained release deslorelin acetate<sup>a</sup>-treated mares and 15% for controls. In addition, the 95% confidence interval around the mean interovulatory interval was 20.8 to 24.8 for sustained release deslorelin acetate<sup>a</sup>-treated mares and 21.1 to 28.3 days for controls. Pregnancy rates after 3 cycles did not differ between treated mares and controls (81%, 83%). Foals born to both treated and control mares were considered normal.

### 4. Discussion

The percentage of mares ovulating within 48 hours is a common measurement made when evaluating the ability of a drug to induce ovulation in mares. Based on the two dose studies, the dose of 1.8 mg

was chosen as the dose of deslorelin acetate that was used in the multicentered clinical trial and is the packaged dose for the commercial product. This is similar to the dose of the compounded deslorelin products and that of the commercial deslorelin acetate implant<sup>b</sup> (2.1 mg). Using this dose, the percentage of mares ovulating in 48 hours was 90% in the controlled studies and 72% to 92% in the clinical trial. These percentages are similar to what has been reported for hCG,<sup>3,4</sup> deslorelin acetate implant,<sup>5</sup> and injectable deslorelin.<sup>6</sup> There was no increase in interovulatory interval after injection, as has been reported previously for deslorelin implants. This may be because of the shorter period of time that this product is released from the site of injection. In another study (Squires, unpublished), concentrations of FSH were measured in diestrus after the injection of the product and were found to be similar to those of control mares, which may also explain why the interovulatory interval was not extended even though mares in that study were given deslorelin acetate<sup>a</sup> for 3 consecutive cycles. This is in contrast to the suppression in FSH concentrations that were reported in mares given deslorelin acetate implant.<sup>1</sup>

In conclusion, a single IM injection of 1.8 mg of deslorelin acetate<sup>a</sup>, suspended in sucrose acetate isobutyrate (SAIB) propylene carbonate, to cyclic estrous mares with pre-ovulatory follicles between 30 and 40 mm was effective in inducing ovulation in 48 hours after treatment. The length of the interovulatory intervals between estrous cycles for mares not pregnant was not altered, and the pregnancy rate of the treated mares was similar to the placebo mares.

Studies were funded by CreoSalus, Louisville, KY. Dr. Squires serves as a consultant for Bioniche Animal Health, the distributor of SucroMate™.

### References and Footnotes

1. Farquhar VJ, McCue PM, Carnevale EM, et al. Deslorelin acetate (Ovuplant) therapy in cycling mares: effect of implant removal on FSH secretion and ovarian function. *Equine Vet J* 2002;34:417–420.
2. Carnevale EM. The mare model for follicular maturation and reproductive aging in the woman. *Theriogenology* 2008; 69:23–30.
3. Sullivan JJ, Parker WG, Larson LL. Duration of oestrus and ovulation time in nonlactating mares given human chorionic gonadotropin during three consecutive cycles. *J Am Vet Assoc* 1973;162:895–898.
4. Blanchard TL, Brinsko SP, Rigby SL. Effect of deslorelin or hCG administration on reproductive performance in first postpartum mares. *Theriogenology* 2002;58:165–169.
5. Stich KL, Wendt KM, Blanchard TL, et al. Effect of a new injectable short-term release deslorelin in foal-heat mares. *Theriogenology* 2004;62:831–836.
6. Burns PJ, Fleury JJ, Gibson J, et al. Evaluation of the Saber™ delivery system for controlled-release of deslorelin acetate for advancing ovulation in mares. *Theriogenology* 1998;49:256.

<sup>a</sup> SucroMate™ Equine, CreoSalus, Inc., Louisville, KY.

<sup>b</sup> Ovuplant™, Peptech Technologies, Sydney, Australia.