

Study Title: A Phase II Study to Evaluate the Delay in Ovulation Following Oral
Levonorgestrel plus Meloxicam Compared to Placebo in Obese but
Normal Menstruating Women

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Statistical Design and Power: We expect that two doses of a levonorgestrel/meloxicam combination 48 hours apart with the first dose administered when the dominant follicle has reached 17 ± 1.0 mm in size, will result in the “Day of Follicular Luteal Transition” (DFLT) being delayed by ≥ 7 days versus the time to DFLT when a woman received two doses of placebo, ≤ 3 days. The DFLT will be determined using changes from the daily urine analyzed for luteinizing hormone, and conjugated metabolites of estrone/estradiol and progesterone. Survival analysis/LogRank method was applied to calculate the required sample size. The outcome event is the time until ovulation (DFLT) and censored observations (subjects for whom ovulation did not occur during the 10-day follow up time) are probable. The aim is to compare the survival curves for the placebo group and the 2-doses treatment group using the length of follow-up for each patient utilizing the Kaplan-Meier method and Log-Rank analysis. The Null Hypothesis is that there will be no significant difference between the two survival curves. The sample size is obtained for a power of 80% and a two-sided test size alpha of 5%. We assume that the ovulation rate in the placebo group is approximately 100% by 10 days after the first dose of placebo. If we want to increase the success rate, the delay in ovulation by ≥ 7 days after the first dose from 5% in the placebo group to $\geq 90\%$ in the treatment group we will need to recruit to complete 21 subjects. We will enroll 26 or more participants to complete 21 participants. Secondary outcomes of changes in blood pressure over time in relation to treatment cycles will be analyzed using Multivariate Analysis of Variance (MANOVA) methods at Days 9/10, 12, and 13. Any relationship between baseline blood pressure and unscheduled bleeding will be analyzed using chi-square or fisher’s exact test in the case of small sample size.