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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Study Protocol: We will perform a single-site, single blind clinical trial to determine the delay in ovulation following administration of a placebo or levonorgestrel plus meloxicam in obese, normally menstruating women aged 18 to 40. The Hypothesis is: *There will be a delay of ≥ 7 days between the first dose of the combination drug, and the occurrence of ovulation compared to ≤ 3 days following placebo.*

We will screen 26 potential participants to enroll and complete 22. Each participant, after signing an Informed Consent and meeting all inclusion and exclusion criteria, will begin Pre-Treatment Visits on menstrual day 9 of the subsequent menstrual cycle following a negative urine pregnancy test. The participant will undergo a transvaginal ultrasound on menstrual days 9, 11, 13, and possibly day 14 to determine ovarian follicle diameters in two planes (frontal and sagittal) using transvaginal ultrasound. When the largest follicle diameter is 16-18 mm, the participant will be given the assigned intervention. Placebo tablets will be given in two doses, 48 hours apart, in the 1st control cycle, and levonorgestrel 1.5 mg plus meloxicam 15 mg two doses 48 hours apart in the 2nd treatment cycle. Each participant will be asked to collect a first morning voided urine sample beginning on menstrual day 9; she will continue to collect daily morning urines for 10 days after the participant is given the first dose of the assigned intervention. The ovarian follicle diameter of 17 mm occurs approximately in the middle of the woman's **window of fertility,** which is the four days preceding the day of ovulation. We anticipate that ovulation will take place within 72 hours after the first placebo dose in >90% of the participants and will be delayed ≥7 days following the first dose of levonorgestrel 1.5 mg and meloxicam 15 mg orally in ≥85% of the participants.

The primary outcome: The primary outcome is the delay in days from the first dose of medication to evidence of ovarian corpus luteum formation resulting from ovulation. The daily urine samples will be assayed for luteinizing hormone, estrone-3-glucuronide, and pregnadiol-3-glucuronide by our central laboratory. Changes in the urinary metabolites of estrone (estrone-3-glucuronide) and progesterone (pregnanediol-3-glucuronide) are used to identify the day of the luteal-follicular transition (DALT), indicating ovulation. Urine luteinizing hormone will be analyzed on a subset of the daily urine samples to confirm an LH increase or surge in the placebo cycle (Days 12 to 17) and the delay, if any, of the LH surge in the levonorgestrel plus meloxicam cycle (Days 12 to 19). These results will be compared to those from our current clinical trial in normal-weight women.

Secondary outcomes: Safety parameters consisting of blood pressure and pulse obtained at each visit, and the incidence of treatment emergent adverse events and any unscheduled vaginal spotting or bleeding captured by the participant using a daily diary card. The participant will be instructed to write down any symptoms or problems along with medications taken, including the study drug and other medications. The occurrence, percentage, and relationship of minor and moderate adverse events will be noted and categorized using Medical Dictionary for Regulatory Activities (MedRA) adverse event classification for each intervention, placebo, and medication, and listed in all reports and publications. Each participant will have their blood pressure and pulse obtained at every visit after sitting for 5-10 minutes. Adverse events and any resulting interventions will be assessed at each visit. Mean and standard deviation of all vital signs results and the incidence of adverse events before and after treatment will be compiled and listed in all reports and publications.