Symbiomix Therapeutics, LLC (Symbiomix) is developing SYM secnidazole in a containing overnight fast, SYM secnidazole in pudding, yogurt, or applesauce to healthy female subjects. A total of 24 female subjects were enrolled to ensure that 18 subjects completed the study. Subjects underwent screening procedures to determine eligibility and were randomized to receive 1 of 3 treatments according to a pre-specified randomization scheme. Subjects in each treatment group were kept in the clinical research unit from Day 1 through Day 5 of each study period for assessments and observation. On Day 1 of each study period, after fasting overnight for at least 10 hours, subjects received the assigned treatment. No additional food was allowed for 4 hours after study drug administration. There was a washout period of at least 7 days prior to the start of the next study period for all subjects. Serial blood samples were collected over 96 hours to determine secnidazole plasma concentrations. A non-compartmental analysis was performed and the PK parameters for each treatment group were reported. Bioequivalence was determined based on the 90% confidence interval criteria for Cmax, AUClast, and AUCinf. Safety assessments and vital signs (seated blood pressure and heart rate) were performed at specified time points during each treatment period and at the conclusion of the study. Safety assessments were performed at specified time points during each treatment period and at the conclusion of the study. Vital signs (seated blood pressure and heart rate) were obtained in each period. The PK data for secnidazole following single-dose administration of SYM-1219 granules in pudding or yogurt are bioequivalent to that of SYM-1219 granules administered in applesauce. The statistical analyses demonstrated bioequivalence between SYM-1219 granules in pudding or yogurt and SYM-1219 granules in applesauce. The 90% confidence intervals for secnidazole AUC0-∞, AUCmax, and Cmax were contained within the 80-125.00% bioequivalence limits. There were no deaths, SAEs, or subject discontinuations due to AEs in this study. Overall, the majority of TEAEs were mild in severity and considered possibly drug related by the PI. There were no clinically significant abnormalities in clinical laboratory, vital sign, ECG, or physical examination findings.

Methods

The present study was designed to assess the bioequivalence between SYM-1219 granules containing 2 g of secnidazole administered under fasting conditions in 3 different foods: pudding, yogurt, or applesauce. Analysis of plasma concentrations characterized the antimicrobial spectrum of secnidazole from the SYM-1219 formulation. Bioequivalence was based on the criteria under the plasma concentration–time curve (AUC) and Cmax, to determine the extent and rate of drug absorption, respectively. Bioequivalence is demonstrated for the 2 comparisons of interest (pudding vs applesauce and yogurt vs applesauce), then patients would be able to choose between these 3 foods based on personal preference for administration of SYM-1219 granules.

Methods

This was an open-label, randomized, 3-way crossover study of SYM-1219 granules, containing 2 g of secnidazole, administered to healthy female volunteers (N=24). Following an overnight fast, SYM-1219 was administered in pudding, yogurt, or applesauce. Subjects underwent screening procedures to determine eligibility and were randomized to receive 1 of 3 treatments according to a pre-specified randomization scheme. SYM-1219 granules were administered in pudding or yogurt (loading treatment) 40 minutes prior to the single oral dose of SYM-1219 granules in pudding or yogurt. Subjects were kept in the clinical research unit from Day 1 through Day 5 of each study period for assessments and observation. On Day 1 of each study period, after fasting overnight for at least 10 hours, subjects received the assigned treatment. No additional food was allowed for 4 hours after study drug administration. There was a washout period of at least 7 days prior to the start of the next study period for all subjects. Serial blood samples were collected over 96 hours to determine secnidazole plasma concentrations. A non-compartmental analysis was performed and the PK parameters for each treatment group were reported. Bioequivalence was determined based on the 90% confidence interval criteria for Cmax, AUClast, and AUCinf. Safety assessments and vital signs (seated blood pressure and heart rate) were performed at specified time points during each treatment period and at the conclusion of the study. Safety assessments were performed at specified time points during each treatment period and at the conclusion of the study. Vital signs (seated blood pressure and heart rate) were performed in each period. Actual sample times were used in the calculations. For the calculation of the PK parameters, plasma concentrations below the limit of quantification (BLQ) prior to the first quantifiable concentration were set to 0.05 and plasma concentrations BLQ after the first quantifiable concentration were treated as missing.

Results

The pharmacokinetics of secnidazole following oral administration of SYM-1219 granules in pudding or yogurt are bioequivalent to that of SYM-1219 granules administered in applesauce. Based on the results of this study, SYM-1219 granules containing 2 g of secnidazole can be administered in either pudding, yogurt, or applesauce. A single oral dose of SYM-1219 granules containing 2 g of secnidazole administered in pudding, yogurt, or applesauce was safe and generally well tolerated in healthy female volunteers.

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