PHENTERMINE/TOPIRAMATE TO END OBESITY AND URIC ACID STONES TRIAL (POUND OUT)

Statistical Analysis Plan - NCT04621929

DECEMBER 17, 2021

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

This is a limited feasibility study using a small control group to compare outcomes. Therefore, the statistical approach is relatively straightforward.

9.4.2 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT(S)

We will conduct both parametric and nonparametric tests. To compare kidney stone growth between baseline and 18 month within treatment group, we would use paired samples t-test and Wilcoxon signed rank sum test. To compare the kidney stone size at 18 month change from baseline between treatment and control group, we will fit an ANCOVA model with the baseline kidney stone size included as an independent variable (ANCOVA is more efficient than ANOVA). Alternatively, we will also conduct non-parametric test by using permutation test.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

We will use a mixed effects model to take into account the correlation among observations within each subject. In this pilot study with small sample size, within group comparison would adopt ANCOVA model and evaluate the treatment effects at each fixed time point for those repeatedly measured outcomes and include the baseline of the dependent variable and other factors such as BMI and age in the model. To compare secondary efficacy end points between groups, pairwise comparisons will be made using contrast statements within the framework of ANOVA with treatment group as a factor.

9.4.4 SAFETY ANALYSES

As the study is single site and involves an FDA-approved drug administered to non-high risk individuals, a local Data and Safety Monitoring plan will created through UF CTSI. A local Safety Officer (Dr Diana Barb) will serve in a safety advisory capacity to monitor participant safety, evaluate the progress of the study, review procedures for maintaining the confidentiality, quality, management, and analysis of the data and data collection. Due to the small number of participants, no additional safety analysis of data is required unless specified by UF IRB or the requesting agency.

9.4.5 BASELINE DESCRIPTIVE STATISTICS

The study groups will be compared at baseline for important demographic and clinical characteristics (including outcome variable) to assess similarities. Continuous variables will be summarized for each group by the mean and standard deviation. For an asymmetrical data, the median and a centile range (such as the 25th and 75th centiles) will

be given. Simple paired t-test will be used to compare means of two related observations (i.e., before-after per subject) while independent sample t-test will be used to compare means of two independent groups. Correlation statistics will be used to measure linear association between two continuous variables while simple linear regression will be used to observe the linear relationship between our predictors and outcome variable.

9.4.6 PLANNED INTERIM ANALYSES

As this is a feasibility study, there are no planned interim analyses.

9.4.7 SUB-GROUP ANALYSES

Due to the small number of recruits, there will be no sub-group analyses performed.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Individual participant data will be collected and compared by use of paired t-test or mixed effects model to take into account the correlation among observations within each subject.

9.4.9 EXPLORATORY ANALYSES