

Cardiometabolic Disease and Pulmonary Hypertension

NCT03349775

Document Version 1/15/2021

Statistical Analysis Plan

For METCPET clinical trial interim analysis

Distributions and outliers of continuous variables will be examined using histograms and Whisker box plots. Variables with skewed distribution will be natural log-transformed to approximate normal distribution. Outliers detected by box plots will be examined case-by-case to ensure no data input errors. Categorical variables (race and ethnicity) will be checked manually in all subjects (n=15). Covariate data including age, sex, race/ethnicity, height in inches, weight in pounds, Body Mass Index (BMI), heart rate, systolic blood pressure, diastolic blood pressure will be summarized and reported in mean (Standard Deviation) for continuous variables and frequencies (percentage) for categorical variables. Between-group differences will be compared using two independent samples t-test or Fisher's exact test as appropriate.

We will calculate PAP/CO slope by using serial pulmonary artery pressure (PAP) and cardiac output (CO) measurements before and after Metformin treatment for each randomized subject. Change in PAP/CO slope will then be generated by subtracting pre-treatment PAP/CO from post-treatment PAP/CO. The primary analysis will be between-group comparisons in PAP/CO slope change pre- and post-treatment in an intention-to-treat analysis using Welch's t-test or Two independent samples t-test depending on the variances in both groups. We will also conduct secondary analysis on other hemodynamic and gas exchange variables with the same procedures. Mean change differences between groups will be reported with 95% confidence interval, and between-group PAP/CO slope changes and mean PAP changes will be visualized using Whisker box plots. P values are two-sided with a significance level of 0.05. All statistical analyses will be performed in SAS 9.4 (Cary, NC).