Statistical Analysis Plan

Naloxone for Optimizing Hypoxemia of Lung Donors (NO-HOLDS)

NCT02581111

Date: August 14, 2015

Prospectively collected data included baseline and follow-up ABGs (closest to six hours after drug administration and final ABG prior to procurement), as well as whether lungs were transplanted (with reasons for non-utilization, if not transplanted). These data were collected at the time of case management by Organ Procurement Coordinators and entered into a centralized study database by the site coordinator. Primary outcome measure was change in PaO2:FiO2 ratio (PFR, calculated by dividing PaO2 from ABG by FiO2) from baseline to final ABG. Secondary outcomes were early change in PFR (from baseline to first repeat ABG) and whether lungs were transplanted from each subject. Additional demographic and clinical data on donors were then abstracted from the OPO donor management databases following the Scientific Registry of Transplant Recipients (SRTR) standard data variables (used to calculate expected organ utilization rates). This additional data included important covariates used for adjustment of our primary and secondary endpoints, including donor age, blood type, smoking history, and positive serologies that could impact lung utilization.

Based on limited available data, we estimated that naloxone would increase PFR compared to placebo by at least 25 mm Hg.[11] This resulted in a sample size of 100 subjects per group required to provide 80% power to detect such an effect size. Effect of randomization group (naloxone vs. placebo) was analyzed using Mann-Whitney U test for PFR and Chi-square test for rate of lungs transplanted. Binary logistic regression was utilized to adjust the effect of treatment group for relevant covariates. Analysis of variance was used to evaluate for between OPO differences. Primary analyses were performed using intention-to-treat principles, but we also evaluated outcomes in a per-protocol analysis including only donors with baseline hypoxemia who received study drug as planned.