Statistical Analysis Plan for Protocol

"Cathelicidin and Vitamin D: Impact on Populations At-Risk and with COPD" (NCT02464059)

Version 27 April 2020

This document serves as an addendum to the approved protocols related to NCT02464059 ["Cathelicidin and Vitamin D: Impact on Populations At-Risk with COPD" (Protocol version 1.2; 9/6/17; IRB 16-2200) and "Cathelicidin and Vitamin D: Impact on Populations with COPD (Protocol 8/23/17; IRB 17-2170)" to outline the detailed statistical analysis plan for the prespecified outcomes of this study. In the event that information in this document is discrepant from the original protocols (as it relates to endpoints or analyses), this detailed statistical analysis plan supersedes the original protocols.

Analysis populations

Full analysis set (FAS): All screened patients with informed consent and at least baseline bronchoscopy.

Descriptive Summary of Study Cohort

Using the FAS, the following variables will be summarized using descriptive statistics (mean and standard deviation, min, max, median) and graphical displays (boxplots, histograms) as appropriate.

- Demographics and clinical variables
- Baseline pre- and post-bronchodilator spirometry measurements

Specific pre-defined outcomes are defined below along with the planned analytical approach.

1.1. Primary Outcomes

1.1.1. Change from Baseline in Lung Cathelicidin Level at 8 Weeks [Time Frame: Baseline and 8 weeks

- Change from baseline to 8 weeks in bronchoscopic lavage lung cathelicidin levels after vitamin D supplementation (comparison between pre- and post-supplementation cathelicidin levels using paired t-tests for repeated measures)

2.1. Secondary Outcomes

2.1.1. Change from Baseline in Blood Cathelicidin at 8 Weeks [Time Frame: Baseline and 8 weeks]

- Change from baseline to 8 weeks in blood cathelicidin levels after vitamin D supplementation (comparison between pre- and post-supplementation cathelicidin levels using paired t-tests for repeated measures)

Analysis plan

Paired sample (dependent) t-test to evaluate for differences in BAL cathelicidin (primary outcome) and plasma cathelicidin (secondary outcome) between pre- to post-vitamin D supplementation. Specifically, we will compare mean cathelicidin levels (log transformed as needed for normality) from pre- and post-supplementation BAL samples, and separately from plasma samples. P-values and 95% confidence intervals will be calculated for all estimates.

All tests with p value < 0.05 will be interpreted nominally as statistically significant. There will be no imputation for missing data.