

Study Title

Effect of Gamma Tocopherol Enriched Supplementation on Response to Inhaled O₃ Exposure

NCT number NCT02911688

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Statistical Analysis Plan

For

Effect of Gamma Tocopherol Enriched Supplementation on Response to Inhaled O₃ Exposure

Statistical Analysis:

The effect of gamma tocopherol (γ T) on ozone (O₃) response of continuous variables (e.g., PMNs in sputum, cytokines, mucins) will be assessed using the difference pre O₃ values after γ T and placebo dosing for a given variable. To analyze cross-over clinical trial data, graphical presentations will be used to highlight potential order and treatment effects and use rigorous testing to confirm these effects. For these graphical presentations, the two plots that depict period 1 responses against period 2 responses for both arm sequence groups (Placebo-Active and Active-Placebo) will be examined to confirm the presence of absence of period effect. The response centroids of each sequence group will be calculated to determine if a direct treatment effect of γ T exists. These observations will be tested with a paired t-test or Wilcoxon signed rank test, depending on normality of the data, to evaluate the significance level of the treatment, the period and the carryover effects.

For analysis of mucociliary clearance outcomes, linear regression models will be fitted that account for the initial regional lung deposition of radioaerosol (the central-to-peripheral, or C/P, deposition ratio) as a covariate to determine if γ T treatment impacts O₃-induced changes in MCC compared to placebo. Dr. Zhou, the biostatistician for the CEMALB will lead the statistical team overseeing data analysis and guide the statistical analysis.

As an alternative analysis approach, regression modeling techniques will be employed to assess genotype effects (including the GSTM1 null genotype) on response to pollutants. For this study, a linear mixed model approach will be used that considers individual tests in a global, unified way where all data are used at the same time. This method should be more powerful than the two sample t-tests, especially when there is a significant carryover effect. This approach will also allow us to account for the influence of gender, race, BMI, and analysis of the effect of the GSTM1 null genotype on response to O₃ and effect of γ T on this response.

To address potential missing data, we will employ multiple imputation methods to address this issue when appropriate.