Data Analytic Plan

Study Title: Blood Pressure Control in Hypertensive Smokers

NCT: NCT00113074

Approval Date: 09/20/2021

Treatment and Prevention Study
Data Analytic Plan

Overview:
The main statistical analyses will be for the three-group randomized clinical trial with the primary analyses restricted to participants that do not relapse to smoking. Participants who discontinue study participation will be assumed to have relapsed to smoking. Therefore, analyses will be restricted to those with available data.

The primary efficacy endpoints are BP and body weight. Since the aim is to evaluate long-term efficacy, the primary analysis will evaluate treatment effects at 1-year. Analyses will also be conducted to assess changes in BP and body weight at six months. The primary analysis will be restricted to participants that have not relapsed to smoking and who provide follow-up data. Secondary analysis will performed using all participants. The primary analysis will be performed using ANCOVA to assess for treatment effects adjusting for the baseline value of the dependent variable, study site, and any baseline variables found to differ significantly between groups. In all cases, each of the two experimental groups will be compared to the UL group. Since there are two pair-wise treatment comparisons of interest (BPC vs. UL; WGP vs. UL), we will utilize Fisher's least significant difference (LSD) approach to protect against inflation of the experiementwise error rate. An initial omnibus test will be used to test the null hypotheses that all group means are equal. Rejection of the null hypothesis will result in subsequent pair-wise comparisons between treatment groups. Conversely, if the null hypothesis associated with the omnibus test is not rejected, pair-wise comparisons will not be necessary.

Secondary endpoints will include servings of fruits and vegetables per day, dietary fat intake (% of total energy from fat), overnight urinary chloride excretion (mmol/day), and self-reported physical activity (kcal/kg/day). The analyses for the secondary endpoints will be similar to that for the primary endpoints, with groups compared using ANCOVA to assess for treatment effects adjusting for baseline values, study site, and baseline variables found to differ significantly between groups. In all cases, each of the two experimental groups will be compared to the UL group.

Relapse to tobacco use will be analyzed as an exploratory endpoint. At every contact following randomization subjects will be assessed for relapse to tobacco use, with relapse defined as using tobacco on seven consecutive days or using tobacco at least one day per week on two consecutive weeks. This definition is consistent with that proposed by the Society for Research on Nicotine and Tobacco (Hughes et al., 2003). For subjects that relapse, the date of relapse will be defined as the first day of tobacco use in the 7-day or 2-week period. Subjects that discontinue study participation prior to the 1-year follow-up visit, who have not already met relapse criteria, will be assumed to have relapsed to using tobacco. For these subjects, the date of relapse will be assigned as the day following their last study visit. Time to relapse will be analyzed using Cox proportional hazards regression (PROC PHREG) with time to relapse as the dependent variable and intervention group as the independent variable. For subjects that do not relapse to using tobacco, the time to relapse will be censored as of the date of their 1-year follow-up visit. Additional multivariable analyses assessing characteristics associated with relapse to tobacco use will be considered. However, these analyses will be considered exploratory in nature since our ability to perform meaningful multivariable analyses will be dependent on the number of subjects that relapse to tobacco use.

A number of additional analyses will be performed to describe the study characteristics and assess comparability between study groups. Participant adherence will be assessed as percentage of contacts completed and compared between groups using the rank sum test. The percentage of subjects that use other products (or programs) for smoking cessation, blood pressure or weight control will be summarized separately and compared between intervention groups using Fisher's exact test. Changes in hypertension status will be noted and coded as: -1=decrease in status, 0=no change, +1=increase in status; and changes in hypertension medication status will be noted and coded as: -1=decrease in medication, 0=no change, +1=increase in medication. Using these coded variables, changes in hypertension status and medication status will be compared across treatment groups using the Kruskal-Wallis test.

Analyses for phase 1 (smoking cessation):
Although the primary analyses are for the randomized trial, the first phase of this investigation (open-label smoking cessation phase) will provide meaningful data regarding smoking cessation efforts for individuals. For this phase, the primary outcome will be prolonged tobacco abstinence at the final program session (session 4) defined as self-reported abstinence from all tobacco (not even a puff) for the last 14 days, confirmed by expired CO<10 ppm. The percentage of participants that discontinue the program prior to the 4th session will be summarized along with the reason for discontinuation. The overall abstinence rate at the end of the program will be summarized using a point estimate and 95% confidence interval, with subjects that discontinue study participation assumed to be smoking. In addition, logistic regression will be used to perform exploratory analyses to assess potential participant characteristics associated with abstinence at the end of treatment. Participant characteristics considered in this analysis will include: age (years), gender, smoking rate (cpd), and level of nicotine dependence (FTND).