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Medication Development in Alcoholism: Apremilast versus Placebo

Statistical Analysis Plan Date: 01/20/2017

Stat Plan from the 01/20/2017 NIAAA grant that encompasses the apremilast study

Statistical Analysis Plan. Demographic and baseline clinical characteristics will be examined for group differences by Fisher's Exact test for categorical/dichotomous variables and ANOVA for continuous variables. Variables will be tested individually for correlation to each outcome variable by Pearson's product-moment correlation or χ^2, as appropriate. Any variable significantly associated with outcome or differing between treatment groups will be evaluated in all subsequent analyses as a covariate and will be retained if it reduces the residual variance, or otherwise will be left out of the model. Potential covariates of interest include baseline value of a measure, baseline values of peripheral markers of inflammation and stress response, sex, family history of alcoholism, smoking, and age of onset of heavy drinking.[98,99,100] ***Hypothesis: Subjects treated with active drug (apremilast) will report significantly lower VAS craving ratings in response to*** *in vivo* ***alcohol cues during human lab testing than placebo treated subjects.*** Repeated measures mixed effects models (MEM)[101] will be used to examine drug-placebo differences in VAS craving ratings in response to beverage exposure (alcohol vs. water), where drug is treated as a fixed, between-subjects variable and beverage presentation is the repeat measure. Beverage will be considered a fixed, within-subjects variable and subject as a random effect. Drug effects on **naturalistic secondary outcomes, i.e., drinking**, will be examined using repeat MEM, as above ***Safety evaluations:*** Rates of treatment-emergent signs and symptoms will be computed for each treatment group by body system (e.g., liver, hematologic). Changes and trends in laboratory results will be examined based on shift tables and scatter plots. Relationship to exposure (dose and time) to study drug will be examined. χ^2 analyses will be used to compare the drug groups on rate of study discontinuation due to adverse reactions and overall.