Official Title in ClinicalTrials.gov: Treatment for Nicotine Addiction in Women

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<from originally planned analysis section- from grant>

Sample Size Considerations and Data Analysis
Power Analysis: As this is the first randomized clinical trial evaluating the effect of tolcapone on withdrawal, smoking urges, and cognition in women smokers during abstinence, we used effect sizes from comparisons of Val158Met genotype as general proxies for treatment differences. In previous research, we found significant differences in women smokers by Val/Val vs. Met/_ genotype in withdrawal ($F= 5.7$, df=48, $p=.02$), smoking urges ($F= 16.9$, df=48, $p<.001$), and sustained attention ($F=9.9$, df=48, $p=.003$) during abstinence, and subjective ratings of nicotine's anxiolytic effects ($F=3.7$, df=47, $p=.02$) (see Preliminary Data). Using G*Power, we found that with a sample of 60, alpha=.05, power=.80, we would be able to detect large effects for our planned analyses ($f=.37$). We expect to enroll 80 subjects to achieve a completion N=60. However, with N=52 we would still be able to detect a large effect size ($f=.40$).
Analysis Plan: The primary statistical models will be analysis of covariance (ANCOVA) to test for medication group differences in withdrawal, smoking urges, sustained attention and smoking choice post-abstinence. COMT genotype will be used as an independent variable in an exploratory two factor ANCOVA. Menstrual cycle phase, race and baseline smoking severity will be included as covariates.
Specific Aim 1: ANCOVAs will examine the effect of tolcapone on reducing a) withdrawal severity (MNWS); b) smoking urges (BQSU); and c) cognitive impairment (e.g., CPT) during abstinence vs. placebo. With 80% power, we can detect a large medication effect ($f=.37$).
Specific Aim 2: ANCOVA will examine the effect of medication vs. placebo on laboratory smoking choices post-abstinence. With 81% power, we can detect a large effect ($f=.40$).
Exploratory Aim 1: ANCOVAs will examine the effect of Met/_ genotype on reduced a) withdrawal severity (MNWS); b) smoking urges (BQSU); and c) cognitive impairment (e.g., CPT) during abstinence vs. Val/Val. With 80% power, we can detect a large genotype effect ($f=.37$).
Exploratory Aim 2: ANCOVA will assess withdrawal and smoking post abstinence, using both medication and genotype as the independent variables and co-varying for baseline scores, to test for a medication by genotype interaction. With 81% power, we can detect a large effect ($f=.40$).
Exploratory Aim 3: Structural equation modeling will examine moderating effects of gonadal hormone levels on withdrawal severity and smoking behavior post-abstinence. The mediation effect size is unknown.