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STATISTICAL APPROACHES IN AN ADAPTIVE CLINICAL TRIAL FOR METHAMPHETAMINE USE DISORDER

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ABSTRACT:

Issues related to moderate-to-high rates of placebo response arise in clinical trials in various disease areas such as depression, pain, addiction, allergy and asthma. In such scenarios, innovative and alternative designs such as adaptive designs incorporating pre-specified interim analyses for futility or efficacy are often considered. In a recent multisite, double blind, adaptive, placebo-controlled trial the PI selected a sequential parallel comparison design (SPCD) to mitigate several threats to the conduct of an efficient efficacy and safety evaluation of extended-release injectable naltrexone plus oral extended-release bupropion in adults with moderate or severe methamphetamine use disorder. SPCD involves a two-stage design, with a larger sample randomized to placebo versus active combination (ratio 1:3) in stage 1 with placebo non-responders from stage 1 re-randomized to active combination versus placebo in a 1:1 ratio in stage 2. The treatment effect was defined as the weighted average of the treatment difference in responder rates in the two stages. The weight and stage 1 randomization allocation factors were obtained by optimizing the power of the test. In the context of an adaptive design, we discuss the statistical topics encountered during the

implementation of this SPCD trial including study blinding, assessment of operating characteristics, interim efficacy analysis, and evaluation of interactions. Simulation results evaluating the operating characteristics (type I error and power) under different scenarios will also be presented.

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