Buprenorphine Stabilization and Induction onto Vivitrol for Heroin-dependent Individuals

Statistical Analysis Plan

August 17, 2017

Primary objective
Individuals dependent on heroin have low rates of successful transition onto the Vivitrol on an outpatient basis. We propose to evaluate novel procedure to initiate treatment with Vivitrol in this difficult to treat population. Participants will be stabilized on buprenorphine for three weeks followed by a rapid induction onto Vivitrol using escalating doses of oral naltrexone.

Primary Endpoint
The primary outcome measure will be the proportion of patients successfully retained to receive the first naltrexone injection (dichotomous).

Secondary Objective
It is not known which factors predict, mediate, and moderate treatment response. Therefore, we propose to collect additional measures that may reflect the physiological changes associated with opioid withdrawal and naltrexone induction as well as response to medications. We will also evaluate the impact of concurrent substance use on treatment outcome and finally evaluate the safety of proposed protocol

Secondary Endpoint
Secondary Outcomes: 1) The proportion of patients successfully retained to receive second and third Vivitrol injection (dichotomous); 2) Measures of opiate withdrawal and sleep (continuous, longitudinal); 3) Measures of mood and anxiety (continuous, longitudinal); 4) Adverse events and serious adverse events; 5) A summary measure (combining urine and self-report) reflecting urine-confirmed abstinence from opioids and urine-confirmed abstinence from other drugs.

Exploratory Objectives
We will explore which patients are most likely to benefit from this procedure. We will evaluate the feasibility and acceptability of the protocol. We will evaluate whether proposed doses of adjunctive medications are adequate.

Hypothesis
We hypothesize that a short-term treatment with buprenorphine prior to initiating treatment with naltrexone will increase the proportion of heroin-dependent patients successfully inducted onto Vivitrol. We hypothesize that at least 65% of patients will be successfully retained to receive the first naltrexone injection. Based on our experience with various induction methods a response rate of less than 45% is too low to warrant further study of this treatment approach.

Analysis Plan
Given this is a single arm efficacy trial, most of the outcomes will be expressed as descriptive statistics. The primary aim is to determine if there is sufficient efficacy for the proposed procedure to warrant future studies.

Sample Size Justification
We believe that 30 participants will allow sufficient number to observe safety and tolerability and to develop precise parameters for the protocol.