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Buprenorphine as Adjunct to Outpatient Induction onto XR-naltrexone (Vivitrol)

Statistical Analysis Plan

NYS PI IRB #7456

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Buprenorphine as Adjunct to Outpatient Induction onto Vivitrol

Study IRB #7456

New York State Psychiatric Institute

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Study Objectives and Endpoints

The primary objective of this pilot open-label study is to evaluate three new outpatient pharmacological procedures to facilitate transition onto a long- acting, injectable form of naltrexone 380 mg (XR-NTX).

The primary aim is to test the feasibility, safety, and effectiveness of the new methods to improve tolerability of naltrexone induction and reducing attrition during detoxification and the first month of naltrexone treatment.

The primary endpoint is the receipt of the two injections of XR-naltrexone given first after completion of the detoxification and induction procedure and the second administered 4 weeks later.

Study Participants and Design

Participants in the study are individuals with opioid use disorder (OUD) who are actively using opioids and are seeking treatment with naltrexone as a relapse-prevention intervention

This is a non-randomized and unblinded trial.

Interested participants will be first screened to determine study inclusion and exclusion criteria. Eligible participants will receive treatment in an outpatient setting and will be consecutively enrolled into treatment with one of the three study procedures: Procedure 1, Procedure 2, and Procedure 3.

Treatment will include following phases: 1) opioid withdrawal management, 2) initiation of naltrexone given orally followed by an injection of XR-naltrexone, 3) Outpatient relapse-prevention treatment, 4) administration of the second XR-naltrexone injection approximately 4 weeks after the first injection.

In addition to pharmacological treatment, all participants will receive a psychosocial intervention that will include elements of motivational interviewing and cognitive-behavioral relapse prevention therapy.

Sample Size

Total enrollment goal is approximately 30 adult participants with OUD. We will enroll the first 10 participants in Procedure 1, the next 10 in Procedure 2, and the last 10 in Procedure 3.

Study Hypotheses

Primary Hypothesis Procedure 1: Adjunctive treatment with buprenorphine 4 mg during the first 5 weeks of naltrexone maintenance will improve opioid abstinence and treatment retention, defined as receiving the second XR- NTX injection.

Primary Hypothesis Procedure 2: Providing buprenorphine 4 mg daily during gradual 9-day titration of oral naltrexone will improve tolerability and success of XR-NTX induction, defined as receiving the first XR-NTX injection.

Primary Hypothesis Procedure 3: Providing buprenorphine 4 mg daily during gradual 9-day titration of oral naltrexone and adjunctive treatment with buprenorphine 4 mg during the first 5 weeks of naltrexone maintenance will improve opioid abstinence and treatment retention, defined as receiving the second XR-NTX injection.

Study Outcome Measures

Procedure 1 and Procedure 3

Primary Outcome measure is the measure of XR-naltrexone initiation success defined as the receipt of two consecutive injections of XR-naltrexone.

Procedure 2

Primary Outcome measure is the measure of detoxification and XR-naltrexone induction success defined as the receipt of the first injection of XR-naltrexone.

Safety of the proposed procedures will be evaluated using a structured instrument for obtaining treatment-emergent adverse effects.

Additional assessment will include measures of residual opioid withdrawal during treatment.

Study Analysis

The primary analysis is a summary statistic of the percent of participants who initiate treatment and receive two consecutive XR-naltrexone injections (Procedures 1 and 3) or the percent of participants who complete detoxification and receive the first XR-naltrexone injection.

In addition, a percentage of patients that received the second injection among those that receive the first injection will also be calculated (Procedure 1 and 3). A summary of the adverse events and serious adverse events will also be presented

Baseline demographic characteristics will be summarized. For continuous variables, descriptive statistics (n, mean, SD, and range) will be provided. For categorical variables, patient counts, and percentages will be provided.