NIDA-CTN-0003

Buprenorphine/Naloxone: Comparison of THREE Taper Schedules for Opiate Detoxification

STUDY OBJECTIVES:

To compare in the outpatient setting, the relative advantages of three rates (7 versus 30 versus 60 days) of buprenorphine-naloxone (BUP/NX) detoxification following four weeks of BUP/NX flexible dosing stabilization. It is hypothesized that a longer detoxification regimen will have greater clinical utility than a shorter regimen regardless of the starting dose of BUP/NX. Safety, treatment retention, withdrawal severity, and opiate abstinence will be explored between the three detoxification regimens to make a recommendation for optimal detoxification with BUP/NX.

STUDY DESIGN:

This is a randomized, open-label, parallel-group design study in which, after screening and baseline assessments are performed, patients will receive a three day BUP/NX induction regimen, a 27 day stabilization and flexible dosing regimen and then will be randomly assigned in a 1:1:1 ratio, after stratifying for dose at day 30, to one of three BUP/NX dose tapering detoxification regimens. Randomization will be stratified within site and according to the flexible dosing dose during stabilization (8, 16 or 24 mg of buprenorphine with 2, 4, and 6 mg of naloxone, respectively). Detoxification in regimen #1 will be performed over 7 days, in regimen #2 over 30 days and in regimen # 3 over 60 days. All patients, regardless of detoxification assignment, will be enrolled in the study for 90 days and continue with treatment as usual at each clinic once each detoxification regimen is completed. The standard counseling procedures used at each clinic, along with self help detoxification handbooks, will be offered to all patients on the study. Patients in each group will be assessed for treatment effect twice weekly during treatment and at follow-up occurring 3 and 6 months after randomization.

STUDY POPULATION:

Three-hundred-sixty (360) patients with Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) criteria for opiate abuse or dependence determined by structured clinical interview (SCID) will be randomized into one of three treatment groups (approximately 120 per group).

ELIGIBILITY CRITERIA:

Treatment seeking males and females, at least15 years-of-age, with a DSM-IV diagnosis of opiate abuse or dependence with the

ability to understand and provide written informed consent will be included. Women of childbearing capacity will be required to use an acceptable method of birth control.

Patients will be excluded if they have any medical condition that would make participation medically hazardous, have known allergy or sensitivity to buprenorphine, or naloxone, or have acute psychosis, severe depression, or immediate suicide risk. Patients who are dependent upon alcohol, benzodiazepines, or other depressants or stimulants, requiring immediate medical attention or who have participated in another investigational study within the last 30 days will be excluded. Patients who have had methadone or LAAM maintenance or detoxification within 30 days of enrollment will also be excluded. Patients who have pending legal actions or for any reason are unable to remain in the area for the duration of detoxification will be excluded.

STUDY INTERVENTIONS:

All patients will receive 4 mg/1 mg BUP/NX with an additional 4 mg/1 mg, if needed on day 1, 8 mg/2 mg BUP/NX on day 2, and 16 mg/4 mg on day 3. Doses will be adjusted on day 4 to 8, 16, or 24 mg depending upon the patient's clinical need. Doses will be continued by adjusting in 8 mg increments between the 8 and 24 mg doses over days 5 to 30. On day 31 patients will be randomized to one of three taper schedules. The BUP/NX taper dose will start at the dose that the patient was receiving on day 30.

DURATION OF THE STUDY:

The total duration of study participation for each patient will be a maximum of 7 months consisting of: screening and baseline; BUP/NX induction, stabliization and flexible dosing (days 0 to 30), detoxification (days 31 to 90); and, follow-up evaluations completed at 3, and 6 months after randomization. It is estimated that 2 patients will be enrolled per site per week with a total of 6 sites. Thus, the estimated length of enrollment is 30 weeks.

SAFETY ASSESSMENTS:

Before any study procedures are performed, patients will be required to provide signed informed consent. All candidates for study enrollment will have a physical examination including vital signs and weight, medical history and history of prior medication use assessment, and psychiatric evaluation including a a checklist for opiate dependence from the structured clinical interview (SCID), a Brief Symptom Inventory (BSI), HIV risk assessment, and clinical laboratory studies (blood chemistry, hematology, Hepatitis B and C serology, and urinalysis) performed during screening/ baseline. Potential participants over the age of 40 or those with a history of cardiovascular disease will have a 12-lead electrocardiograph (ECG). Female patients will be given a pregnancy test at baseline and monthly thereafter during treatment. Assessments of adverse events (AEs) and concomitant medication use will be performed daily during detoxification.

OUTCOME ASSESSMENTS:

Abstinence from opiates, amphetamines, cocaine, cannabinoids, and benzodiazepines will be assessed by urine drug screen measured at baseline, throughout stabilization and detoxification, and at follow-up. Treatment retention will be calculated as the number of days each patient received his/her detoxification medication. The patient's status in the study will be tracked with a Treatment Status Survey (TSS). The amount of ancillary medications will be calculated by dose administered and adjusted according to symptomology (i.e., several medications are permitted for treating anxiety, insomnia, nausea, etc.) during detoxification.

Withdrawal symptoms will be assessed using the clinical opiate withdrawal scale (COWS), the adjective rating scale for withdrawal (ARSW), and visual analog scales (VAS) during treatment and at follow-up (COWS and ARSW only). Additional measures of overall treatment effect will include Addiction Severity Index (ASI), a client satisfaction questionnaire (CSQ), and SF-36 Health-related Quality of Life) measured at baseline, during detoxification and at all follow-up visits.

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