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Efficacy of Buprenorphine/Naloxone Rapidly Dissolving Sublingual Tablets (BNX-RDT) After Switching From BNX Sublingual Film

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Objectives: The aim of the study was to evaluate treatment retention, efficacy, and preference ratings among opioid-dependent patients transitioning between a buprenorphine/naloxone rapidly dissolving sublingual tablet formulation (BNX-RDT) and BNX film.
Methods: After a 2-day, blinded, fixed-dose induction with BNX-RDT (5.7/1.4 mg and 5.7/1.4 or 11.4/2.8 mg, respectively) or buprenorphine (8 mg and 8 or 16 mg, respectively), patients received open-label titrated doses of BNX-RDT or BNX film (generic buprenorphine induction group) during days 3 to 14. On day 15, patients switched treatment (using a conversion ratio of 5.7–8 mg) and continued switched treatment through day 22. Assessments included treatment retention, opioid withdrawal (Clinical and Subjective Opiate Withdrawal scales), opioid cravings (0–100 visual analog scale [VAS]), and preference ratings.
Results: Of the 287 patients who switched from BNX-RDT to BNX film and 279 patients who switched from BNX film to BNX-RDT at day 15, 8.7% and 6.1% withdrew, respectively. Reductions in opioid withdrawal and cravings were similar with both formulations through day 15; after switching treatment, reductions were maintained through day 22 in both groups. Preference ratings at day 22 (patients had received both formulations) favored BNX-RDT for taste, mouthfeel, ease of administration, and overall preference (all $P < 0.0001$).
Conclusions: In both patient groups who switched treatment at day 15, more than 90% were retained in treatment, and reductions in opioid withdrawal and cravings were sustained. A significant majority of patients preferred BNX-RDT over BNX film, the clinical impact of which requires further study.

Key Words: buprenorphine, naloxone, opioid-related disorders, substance-related disorders

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INTRODUCTION

Opioid dependence is a significant public health problem in the United States (Substance Abuse and Mental Health Services Administration, 2013), with estimated annual economic costs exceeding $55 billion as a result of lost workplace productivity and increased healthcare and criminal justice expenditures (Birnbaum et al., 2011). However, successful treatment of opioid dependence using opioid-substitution therapy with long-acting opioids such as buprenorphine can substantially reduce these costs and improve patients' functioning (Lynch et al., 2014; Volkow et al., 2014). A retrospective study of 2 large US health systems found that mean total healthcare costs for opioid-dependent patients receiving buprenorphine treatment and counseling were less than half of the costs for patients receiving little or no treatment ($13,578 vs $31,035) (Lynch et al., 2014).

Effective pharmacologic maintenance treatment approaches reduce opioid cravings, prevent withdrawal, improve treatment retention, and reduce participation in risky behaviors (eg, injection drug use) (Gunderson and Fiellin, 2008; Mattick et al., 2014). Patient engagement in psychosocial and behavioral counseling is recommended in addition to pharmacologic treatment to promote healthy behaviors and self-motivation (World Health Organization, 2009). Individualized treatment plans should address factors that influence recovery, including past treatment history, living conditions, social and cultural factors, and patient acceptance and satisfaction with treatment (World Health Organization, 2009). Of these factors, patient satisfaction with opioid-substitution treatment may be affected by patient perception of the convenience of treatment and sensory properties (eg, taste, mouthfeel) of medication (Osterberg and Blaschke, 2005; Montesano et al., 2010; Fischer et al., 2015). Assessing patient

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satisfaction with treatment is a potential target to improve adherence and maximize the clinical and societal benefits of therapy (Montesano et al., 2010; Tkacz et al., 2012, 2014). Although improved clinical outcomes are understandably the primary goal for mental health treatment interventions, specific patient-focused outcomes may have fundamental value as well, including the importance of patient preference when selecting treatment and patient engagement in clinical decision-making (Kroenke, 2015).

Sublingual buprenorphine and buprenorphine/naloxone (BNX) combinations are effective options for office-based treatment of opioid dependence, with a low potential for toxicity and misuse (Apelt et al., 2013; Lyseng-Williamson, 2013). Zubsolv (Orexo US, Inc., Morristown, NJ) is a buprenorphine/naloxone rapidly dissolving sublingual tablet formulation (BNX-RDT) with improved absorption and bioavailability that was developed as an alternative to sublingual BNX tablet and film formulations (Lyseng-Williamson, 2013). This formulation incorporates sucralose and menthol to mask the bitter taste of active ingredients, has improved bioavailability compared with other sublingual BNX tablet and film formulations, and has a fast dissolution rate (Lyseng-Williamson, 2013; Fischer et al., 2015). A sublingual 5.7/1.4-mg dose of BNX-RDT was found to provide equivalent buprenorphine exposure and 12% lower naloxone exposure than an 8/2-mg buprenorphine/naloxone dose of a previously available BNX tablet (ie, a 30% lower dose of BNX-RDT can be used compared with the previously available BNX tablet) (Lyseng-Williamson, 2013; Fischer et al., 2015). In addition, the availability of multiple dose strengths of BNX-RDT (1.4/0.36, 2.9/0.71, 5.7/1.4, 8.6/2.1, and 11.4/2.9 mg) (Zubsolv Package Insert, 2015) might simplify dosing and allow patients to be treated with fewer tablets daily.

Although patient preference for various buprenorphine products has not yet been proven to influence clinical outcomes and prevent relapse, enhancing patient experience with buprenorphine-based medication has been posited to potentially facilitate treatment engagement (Daulouede et al., 2010; Clay et al., 2014; Teruya et al., 2014), which, in turn, could influence retention in treatment (Tkacz et al., 2012). Regarding preference data for the BNX formulations, in a study of healthy volunteers, BNX-RDT received higher ratings for taste and overall acceptability than BNX film and a previously available BNX tablet formulation (Fischer et al., 2015). In addition, participants reported preferable taste and greater overall acceptability compared with the previously available BNX tablet, and preferable mouthfeel and less unpleasant aftertaste compared with sublingual BNX film (Fischer et al., 2015). Overall, 89% and 77% of participants preferred BNX-RDT over BNX film and the previously available BNX tablet, respectively (Fischer et al., 2015).

Whereas data from healthy volunteers may suggest preferable characteristics of BNX-RDT (Fischer et al., 2015), clinical data with opioid-dependent patients are needed for further validation. Although several studies assessed the efficacy and safety of switching from generic buprenorphine to BNX formulations (Daulouede et al., 2010; Montesano et al., 2010; Stimolo et al., 2010), clinical evidence is lacking with regard to switching between different BNX formulations, including BNX-RDT, which has a 5.7/1.4 mg buprenorphine/naloxone ratio as determined by a pharmacokinetic bioequivalence trial rather than clinical outcome data (Fischer et al., 2015). Hence, comparative data between BNX products are needed to evaluate patient preference and also clinical efficacy. Such data are of paramount importance for patients and clinicians to make informed decisions when selecting treatment. To address these gaps in treatment knowledge, the current study examined the effect of switching treatments between 2 sublingual BNX formulations—BNX film and BNX-RDT—on treatment efficacy, safety, and preference ratings in opioid-dependent patients participating in the Induction, STabilization, Adherence and Retention Trial (ISTART).

METHODS

Study Design

The ISTART was a prospective, randomized, parallel-group, multicenter, noninferiority trial conducted at 43 centers in the United States, from August 2013 to April 2014; the primary efficacy and key secondary outcomes of ISTART were previously reported (Gunderson et al., 2015). The study comprised a 2-day induction phase and a 20-day stabilization phase (Fig. 1). Visits were scheduled on days 1, 2, 3, 4, 8, 15, and 22 (final study visit). Opioid-dependent patients were randomly assigned to induction with either BNX-RDT or generic buprenorphine tablets for 2 days. On day 3, patients allocated to buprenorphine were switched to BNX film, whereas those allocated to BNX-RDT continued on the same treatment. On day 15, patients receiving BNX film were switched to BNX-RDT, and those on BNX-RDT were switched to film. The current study presents secondary analysis data focusing on the phase after the transition between products at day 15. Although patients were stabilized on treatment with sublingual BNX-RDT or BNX film during the first 15 days of the study, patients were evaluated for an additional 6 days after the treatment switch for clinical symptoms of withdrawal, which was anticipated to be an adequate timeframe for such symptoms to occur. Measuring withdrawal after the switch was especially important for patients switched to the higher-bioavailability BNX-RDT

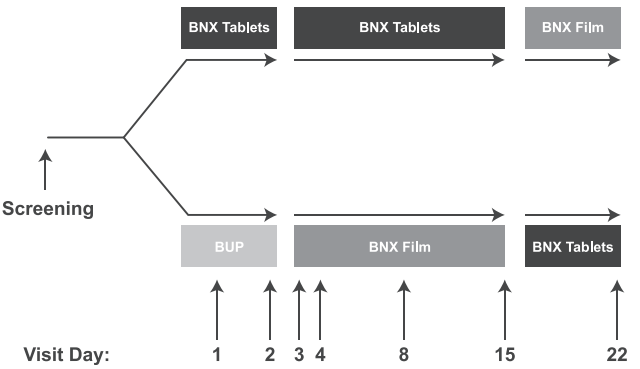

FIGURE 1. Study design. BNX-RDT, buprenorphine/naloxone rapidly dissolving sublingual tablet formulation; BUP, buprenorphine.

formulation, which has a lower dose (derived from pharmacokinetic data) and, until the present study, had not been evaluated in a clinical setting with opioid-dependent patients.

This study was conducted in accordance with the Declaration of Helsinki, and in compliance with the International Council on Harmonisation Good Clinical Practice guidelines and all applicable laws and regulations. The study protocol was approved by an institutional review board at each site, and all patients provided written informed consent. The study is registered on ClinicalTrials.gov (identifier NCT01908842).

Patients

Adults aged 18 to 65 years and in generally good health, who met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR) criteria for opioid dependence in the past 12 months, were eligible if they agreed to abstain from opioid use and other addictive drugs, and if they demonstrated at least mild withdrawal symptoms defined as a Clinical Opiate Withdrawal Scale (COWS) score at least 9 predose on day 1. Eligibility also required a buprenorphine-negative urine drug screen, and for female participants, a negative urine pregnancy test and agreement to use a reliable method of contraception. Any prescribed opioids for pain were withdrawn before induction after obtaining clearance from the prescribing physician.

Patients could not have a serious, untreated axis I DSM-IV-TR psychiatric comorbidity or be considered at risk for suicide; a clinically significant medical disorder or condition that would compromise participant safety or the validity of study results; or a tongue or oral deformity that might affect absorption of study drug. Other exclusion criteria included use of generic buprenorphine monotherapy within 90 days or methadone at a daily dose above 30 mg within the past week, any methadone within 30 hours of initial study treatment, or any medication or product with strong cytochrome P450 3A4 inhibition or induction properties within 14 days of screening.

Study Treatment

Study treatment consisted of BNX-RDT (5.7/1.4 or 1.4/0.36 mg; Zubsolv), BNX sublingual film (8/2 or 2/0.5 mg; Suboxone film, Reckitt Benckiser, Richmond, VA), and generic buprenorphine sublingual tablets (8 or 2 mg; Roxane Laboratories, Columbus, OH). Generic buprenorphine was selected as the comparator agent for induction as it was the only product approved for use as induction therapy when the study was designed and initiated. On days 1 and 2, patients received a fixed dose of BNX-RDT (5.7/1.4 mg on day 1 and 5.7/1.4 or 11.4/2.8 mg on day 2) or generic buprenorphine (8 mg on day 1 and 8 or 16 mg on day 2). On day 3, patients in the generic buprenorphine group were switched to BNX film. During the open-label stabilization period (days 3–22), individual daily dosing regimens could be titrated to a bioequivalent maximum of 17.1/4.2 mg for BNX-RDT and 24/6 mg for BNX film based on clinical symptoms. On day 15, patients switched treatments according to a fixed conversion factor of 5.7 to 8 mg based on the corresponding dose strengths of BNX-RDT and BNX film; patients were switched to a dose commensurate to the dose they were taking in the previous week. Patients continued on the switched treatment though day 22.

Endpoints

The endpoints of focus for the current study were secondary efficacy endpoints assessed during days 15 to 22 of the ISTART. These included retention in treatment at each visit, opioid withdrawal assessed using the COWS (scored from 0 to 48: <5 = none; 5–12 = mild; 13–24 = moderate; 25–36 = moderately severe; >36 = severe withdrawal symptoms) (Wesson and Ling, 2003) and the Subjective Opiate Withdrawal Scale (SOWS; scored from 0 to 64; lower score is indicative of less withdrawal) (Handelsman et al., 1987), and opioid cravings assessed using a VAS ranging from 0 (''no cravings'') to 100 (''most intensive craving I have ever had''). COWS, SOWS, and VAS cravings assessments were performed before dosing on treatment visit days and additionally at 0.5, 1.5, 3, and 6 hours after dosing on day 1. Before treatment on day 22, patients completed a dichotomous preference assessment questionnaire comparing BNX-RDT and BNX film in terms of taste, mouthfeel, ease of administration, and overall preference. The coprimary efficacy endpoints in the ISTART were retention in treatment at days 3 and 15, defined as the number of patients who received treatment on days 3 and 15.

Safety evaluations included assessment of adverse events (AEs) at all visits from day 1 through the end of the study and patient assessment of constipation symptoms (PAC-SYM; measures 12 symptoms in 3 domains [abdominal, rectal, stool] scored from 0 to 4; lower score is favorable) at screening and on days 15 and 22.

Statistics

Efficacy assessments were performed using the full analysis population, which was defined as all patients who were randomized and had at least 1 dose of study medication. Safety assessments were performed using the safety population, which was defined as all patients who had at least 1 dose of study medication. As the coprimary endpoints of ISTART were retention in treatment at days 3 and 15 (Gunderson et al., 2015), the handling of dropouts or missing data was not an issue. All secondary efficacy analyses were based on observed data in the full analysis population.

Data regarding patient demographics and baseline clinical characteristics were summarized descriptively; no formal statistical testing was performed. Patient preference for BNX sublingual tablets versus BNX film in terms of taste, mouthfeel, ease of administration, and overall preference was assessed after the last treatment period using McNemar test. Changes from baseline in COWS and SOWS total scores and VAS cravings assessments were tabulated, but not formally analyzed. AEs were coded using the Medical Dictionary for Regulatory Activities (version 16.0). PAC-SYM results were evaluated using summary statistics for observed values and changes from baseline at days 15 and 22.

RESULTS

Patients

Patient demographic and baseline characteristics were similar between the 2 treatment arms (Table 1). The study cohort had a mean age of 35.6 years; most patients were men

TABLE 1. Demographics and Baseline Clinical Characteristics*

Characteristics	BNX-RDT (n = 383)	Buprenorphine/BNX Film (n = 375)	All Patients (N = 758)
Age, mean (SD), y	35.7 (11.26)	35.6 (11.28)	35.6 (11.26)
Sex, n (%)			
Male	216 (56.4)	236 (62.9)	452 (59.6)
Female	167 (43.6)	139 (37.1)	306 (40.4)
Race, n (%)			
White	318 (83.0)	312 (83.2)	630 (83.1)
Black/African American	51 (13.3)	49 (13.1)	100 (13.2)
Other or not recorded	14 (3.7)	14 (3.7)	28 (3.7)
Duration of opioid dependence, mean (SD), y	10.7 (9.57)	10.5 (9.01)	10.6 (9.29)
Self-report of prior substance use over past 30 d, n (%)†			
Heroin	212 (55.5)	199 (53.4)	411 (54.4)
Methadone	51 (13.4)	48 (12.9)	99 (13.1)
Buprenorphine	41 (10.7)	29 (7.8)	70 (9.3)
Other opioids/analgesics	240 (62.8)	235 (63.0)	475 (62.9)
Self-report of prior substance use in patient's lifetime, n (%)†			
Heroin	235 (61.8)	236 (63.4)	471 (62.6)
Methadone	127 (33.5)	129 (34.7)	256 (34.1)
Buprenorphine	125 (32.9)	108 (29.0)	233 (31.0)
Other opioids/analgesics	304 (79.8)	288 (77.4)	592 (78.6)

*Patient demographics and baseline clinical characteristic data were summarized descriptively; no formal statistical testing was performed.
†Percentages based on number of patients with available responses.
BNX-RDT, buprenorphine/naloxone rapidly dissolving sublingual tablet formulation; SD, standard deviation.

(59.6%) and white (83.1%) with a mean reported duration of opioid dependence of 10.6 years.

A total of 758 opioid-dependent patients were randomly assigned to induction with BNX-RDT (n = 383) or generic buprenorphine (n = 375) (Fig. 2). Of these, 701 patients entered the open-label stabilization phase on day 3 (BNX-RDT, n = 357; BNX film, n = 344). From day 3 to day 15, 135 patients (19.3%; BNX-RDT, n = 70; BNX film, n = 65) withdrew from the study.

At day 15, 287 patients switched from BNX-RDT to BNX film, and 279 patients switched from BNX film to BNX-RDT. From day 15 to day 22, 25 patients (8.7%) who were switched to BNX film and 17 patients (6.1%) who were switched to BNX-RDT withdrew from the study.

Doses of Study Treatment

Based on bioequivalent doses, mean daily doses for both formulations were comparable at day 15 and day 22. For BNX-RDT, the mean daily dose was 10.8 mg at day 15 (15.2 mg film equivalent based on the 8.0:5.7 mg film-to-tablet ratio) and 11.3 mg (15.9 mg film equivalent) at day 22. The mean daily dose of BNX film was 15.9 mg at day 15 and 16.0 mg at day 22.

Patient Preference

Among patients who had received treatment with 1 formulation up to day 15 and with the other formulation from day 15 to 22, preference assessment results significantly favored BNX-RDT ($P < 0.0001$ for each comparison; Fig. 3). For the overall preference assessment, 70.2% (346/493) of patients preferred BNX-RDT and 29.8% (147/493) preferred BNX film ($P < 0.0001$).

Opioid Withdrawal Symptoms

Both treatments similarly reduced opioid withdrawal as assessed by COWS total scores during induction, stabilization, and after switching (Fig. 4A). Similar COWS total scores at day 15 and day 22 in both treatment groups indicated an absence of emergent withdrawal symptoms after switching treatments. At day 15, mean ± standard deviation (SD) COWS total scores were 4.1 ± 3.5 with BNX-RDT and 3.7 ± 3.4 with BNX film, corresponding to mean ± SD changes from baseline of -10.7 ± 4.9 and -11.2 ± 4.8, respectively. At day 22, mean ± SD COWS total scores were 3.3 ± 3.4 for patients switched to BNX film and 3.4 ± 3.3 for patients switched to BNX-RDT, indicating a lack of emergent withdrawal for both groups (COWS < 5) (Wesson and Ling, 2003) and corresponding to mean ± SD changes from baseline of -11.5 ± 4.8 and -11.3 ± 5.0, respectively.

Similarly, reductions in opioid withdrawal over time as assessed by SOWS total scores were comparable between treatment before and after switching (Fig. 4B), further demonstrating a lack of emergent withdrawal symptoms with both formulations after switching treatments. At day 15, mean ± SD SOWS total scores were 7.2 ± 7.7 with BNX-RDT and 6.7 ± 8.1 with BNX film, corresponding to mean ± SD changes from baseline of -24.1 ± 13.8 and -26.6 ± 13.8, respectively. At day 22, mean ± SD SOWS total scores were 7.3 ± 9.2 for patients switched to BNX film and 6.8 ± 7.9 for patients switched to BNX-RDT, representing mean ± SD changes from baseline of -25.6 ± 13.4 and -24.5 ± 14.5, respectively.

Opioid Cravings

Both treatments similarly reduced opioid cravings with a time course comparable to that for the reduction in opioid withdrawal symptoms (Fig. 4C). At day 15, mean ± SD VAS craving scores were 21.6 ± 23.9 with BNX-RDT and 19.1 ± 23.4 with BNX film, corresponding to mean ± SD changes from baseline of -46.8 ± 30.7 and -54.2 ± 28.7, respectively. At day 22, mean ± SD craving scores were 20.9 ± 23.8 for patients switched to BNX film and 20.2 ± 22.9 for patients switched to BNX-RDT, corresponding

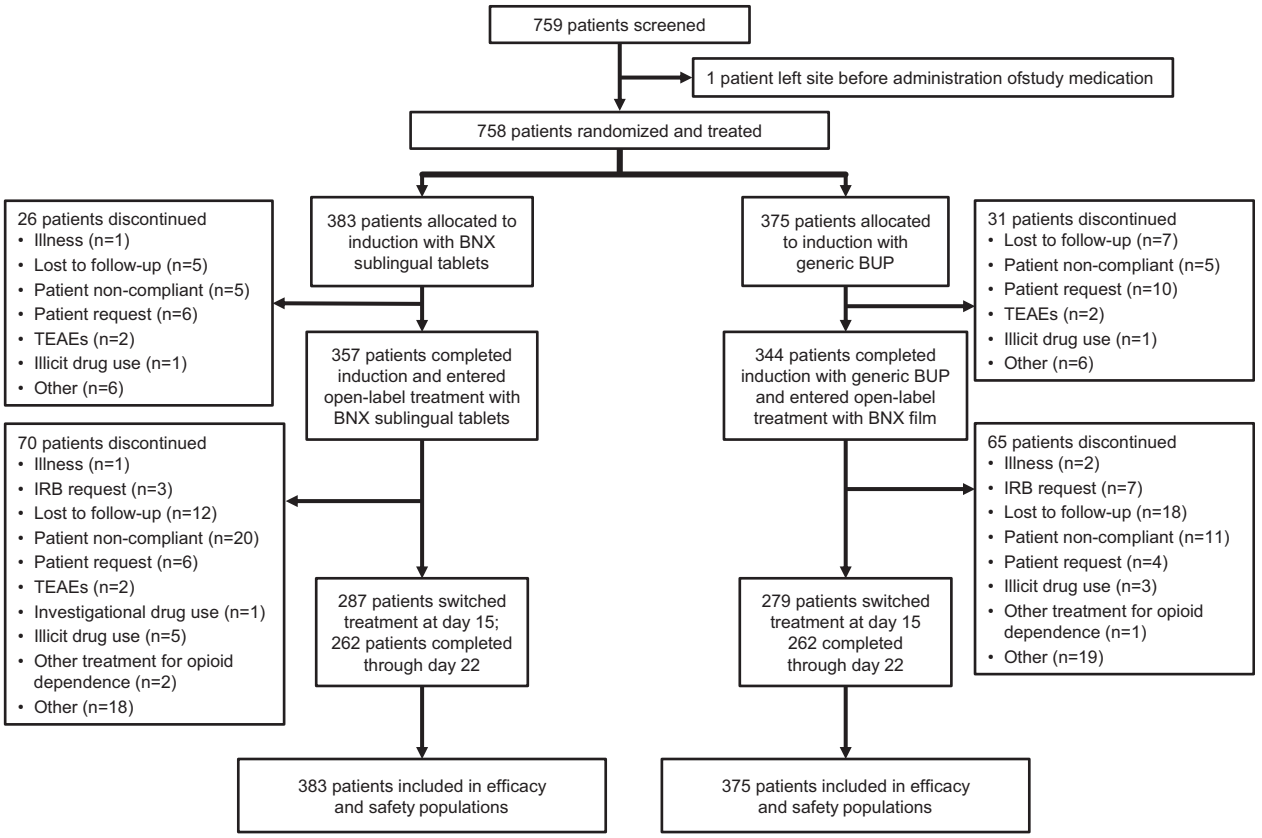

FIGURE 2. Patient disposition. BNX-RDT, buprenorphine/naloxone rapidly dissolving sublingual tablet formulation; BUP, buprenorphine; IRB, Institutional Review Board; TEAE, treatment-emergent adverse event.

to mean ± SD changes from baseline of −52.3 ± 28.8 and −49.0 ± 30.1, respectively.

Safety

During the entire open-label phase, the incidence of treatment-related AEs assessed at the onset of the AE was 8.3% (53/635) with BNX-RDT and 7.5% (47/630) with BNX film. Of treatment-related AEs occurring in patients assessed at the onset of the AE through the end of the study, constipation occurred in 1.9% (12/635) of patients receiving BNX-RDT and 2.2% (14/630) of patients receiving BNX film. During the open-label stabilization phase from days 3 to 15, the incidences of treatment-related AEs in the BNX-RDT and BNX film groups were 11.8% (42/357) and 10.8% (37/344), respectively ($P = 0.67$). The most common AEs were constipation (2.8% vs 3.5%) and headache (1.4% vs 2.0%).

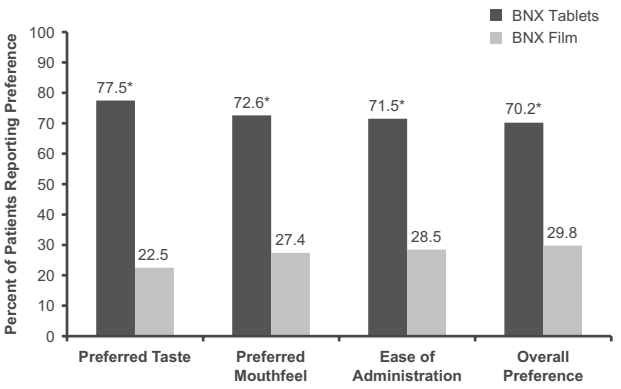

FIGURE 3. Patient preference ratings for BNX-RDT compared with BNX sublingual film at day 22 (full analysis population). BNX-RDT, buprenorphine/naloxone rapidly dissolving sublingual tablet formulation. *$P < 0.0001$ for BNX-RDT vs BNX sublingual film.

Mean changes from baseline in PAC-SYM scores at day 15 and day 22, respectively, were −0.45 and −0.37 for patients stabilized on BNX-RDT, and −0.38 and −0.46 for patients stabilized on BNX film. These results indicate that, on average, constipation symptoms improved over the course of the study with both treatments.

There were no treatment-related serious AEs with either treatment. However, after the day 15 switch, 1 patient in the BNX film group experienced a serious AE of increased transaminase levels deemed unrelated to study medication. This serious AE was considered moderate in intensity and resolved after 6 days.

DISCUSSION

This study indicates that clinical efficacy and safety are maintained when opioid-dependent patients entering maintenance switch between BNX-RDT and BNX film formulations

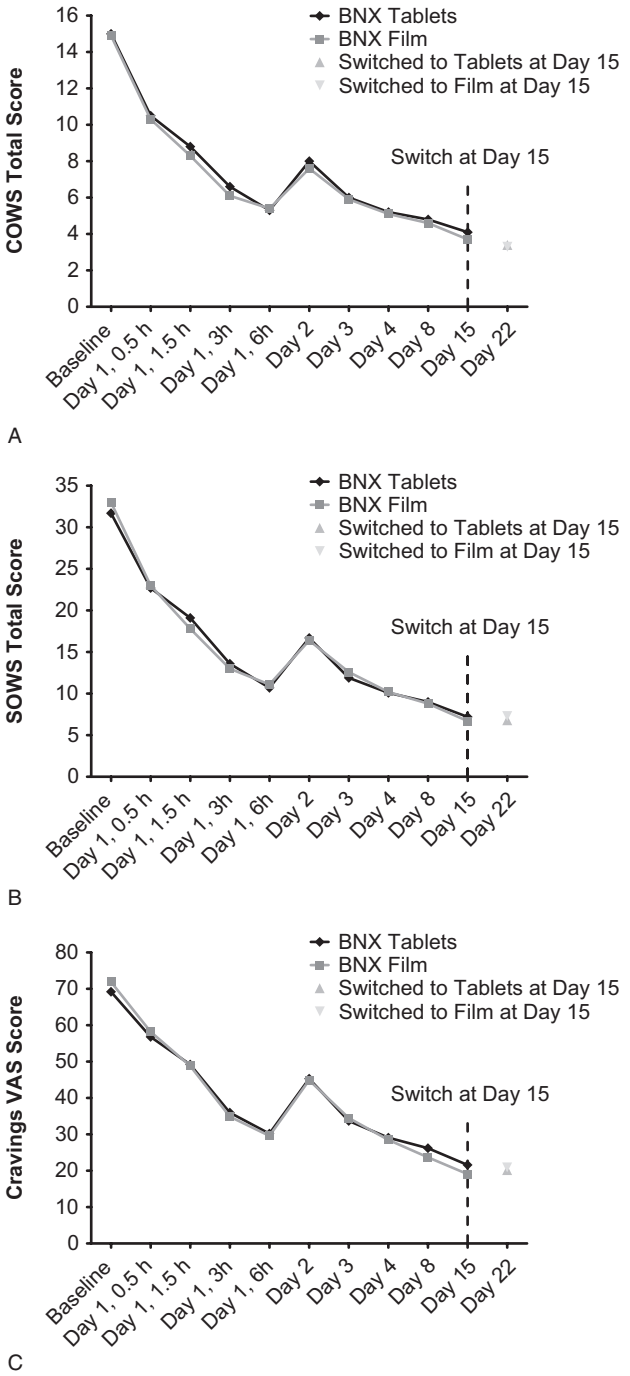

FIGURE 4. Mean time profile of (A) COWS total score, (B) SOWS total score, and (C) VAS score for opioid craving by treatment group (full analysis population). BNX, buprenorphine/naloxone; COWS, Clinical Opiate Withdrawal Scale; SOWS, Subjective Opiate Withdrawal Scale; VAS, visual analog scale.

after completion of a 15-day stabilization period. The findings provide important practical information needed by clinicians and patients when considering a transition between BNX formulations during maintenance treatment, particularly as the more recently available BNX-RDT formulation is a departure from other previously and currently available BNX products in terms of per tablet dose, physical characteristics (eg, taste), absorption, and bioavailability (Lyseng-Williamson, 2013; Fischer et al., 2015). Clinicians and patients alike may question if the 5.7:8.0 mg conversion factor, established based on bioequivalence data, is clinically comparable. Our findings indicate clinical comparability based on continued reduction in opioid withdrawal and cravings. Although most participants preferred the tablet formulation, additional data are needed regarding the potential impact on adherence and longer-term patient outcomes.

Regarding comparable efficacy data, of patients who switched treatments at day 15, more than 90% of patients in both groups completed through day 22 of treatment after switching. Although no formal statistical analysis was performed for patient discontinuations, rates were numerically similar in both treatment groups after the switch (8.7% and 6.1% of patients who switched from BNX-RDT to BNX film or BNX film to BNX-RDT, respectively). Opioid withdrawal and craving results were similar for both formulations at day 15 (before switching), with no indication of a change in symptoms by day 22 after the switch from either product. By day 15, mean COWS total scores in both treatment groups indicated that, on average, patients were withdrawal-free (ie, mean total score <5). Safety results showed that AEs through the end of the study were similar in frequency to AEs recorded from days 3 to 15 before the switch. The incidence of constipation-related AEs was low, and on average, preexisting constipation symptoms improved from baseline to the end of the study for both medications. In addition, titrated doses remained essentially the same based on bioequivalence for both groups from day 15 to day 22, indicating that the 5.7 to 8-mg conversion ratio is appropriate when switching between products.

The efficacy data provide clinical evidence that doses determined to be bioequivalent in a previous pharmacokinetic study (Fischer et al., 2015) are also clinically comparable when transitioning between products (ie, a 5.7/1.4-mg buprenorphine/naloxone dose of BNX-RDT is clinically similar to an 8/2-mg buprenorphine/naloxone dose of BNX sublingual film). Thus, it is noteworthy that comparable efficacy can be expected when patients are treated with an approximately 30% lower dose of BNX-RDT than of BNX film. In clinical practice, patients might express concerns about switching to a lower dose (Lintzeris et al., 2013). To the extent that expectations can influence perceived drug effects (Johanson and Preston, 1998; Kirk et al., 1998; Volkow et al., 2003), the findings from the current study may help alleviate patient concerns about a transition to a lower bioequivalent dose of the tablet formulation and thus avoid a potentially unnecessary dose increase. Although the study indicates efficacy and tolerability when changing between products, practitioners should continually monitor patients for signs of overmedication, withdrawal, or underdosing, as dose adjustments may be necessary when switching treatments (Suboxone Package Insert, 2014; Zubsolv Package Insert, 2015).

A substantial majority ($>70\%$) of patients who had experience with both BNX formulations reported that they preferred BNX-RDT over BNX film in terms of taste, mouthfeel, ease of administration, and overall acceptability.

Previously reported preference data on sublingual buprenorphine-containing products have been mixed. Although patients reported preferring the first approved BNX tablet formulation (Suboxone) over buprenorphine alone in terms of taste, size, and sublingual dissolution time (Daulouede et al., 2010), the palatability of the first BNX tablet formulation received less favorable ratings in a separate study (Montesano et al., 2010). In that study of patients who switched from a buprenorphine tablet to a BNX tablet formulation, approximately 50% of participants reported disliking the sensory properties (taste, color, odor, and mouthfeel) of the BNX tablet.

Previous studies have demonstrated that increased adherence may result in greater clinical benefits, lower relapse rates, and reduced direct healthcare expenditures (Montesano et al., 2010; Tkacz et al., 2012, 2014). Further study in a real-world setting with longer treatment duration is needed to examine if strong patient preference for a BNX formulation will improve adherence and result in better clinical outcomes.

There are several possible limitations of this study. Firstly, patient familiarity with the BNX film formulation could have biased outcomes; however, it seems likely that any bias introduced by previous experience with BNX film might favor that formulation over the higher-bioavailability BNX-RDT. Secondly, this study was conducted at selected clinical research sites, and findings may not be generalizable to all office-based practices. Finally, study treatment was open-label rather than blinded, which was necessary to allow for assessments of patient preference.

CONCLUSIONS

These data indicate that among opioid-dependent patients receiving BNX maintenance treatment, transition between BNX film and BNX-RDT may be undertaken with comparable efficacy and safety. Patient discontinuation rates during the treatment switch phase were similar for each group, and the transition between both products was associated with continued withdrawal suppression, craving reduction, and similar safety profiles. Thus, there is no apparent clinical rationale from the findings indicating limitations when switching patients between the film and tablet products tested in the study. Most patients preferred BNX-RDT over BNX film; however, further study is required regarding the clinical implications of patient preference. Overall, the study provides important data to guide clinical decision-making during buprenorphine maintenance treatment, and hopefully will help mitigate the public health burden of opioid use disorder.

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