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Effects of monthly buprenorphine extended-release injections on patient-centered outcomes: A long-term study

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ABSTRACT

Introduction: The physical, social, psychological, and economic burden of opioid use disorder (OUD) is substantial. As of the year 2019, the predominant focus of OUD research was outcomes such as retention and abstinence. We report herein the effects of extended-release buprenorphine (BUP-XR), the first FDA-approved subcutaneously injected, monthly treatment for OUD, on patient-centered outcomes.

Materials and methods: Patient-centered outcomes were collected during an open-label safety study of participants with OUD (NCT# 02510014) evaluating BUP-XR. Measures collected during the study included the EQ-5D-5L, SF-36v2, Treatment Effectiveness Assessment (TEA), Addiction Severity Index-Lite (ASI-Lite), employment/insurance status questionnaire, and Medication Satisfaction Questionnaire (MSQ). Changes from baseline to end of study week 49 were analyzed using mixed models for repeated measures. "Baseline" was defined as the value collected prior to the first BUP-XR injection. Results presented are for those participants who initiated treatment on BUP-XR during the open-label study and were eligible to receive up to 12 injections.

Results: Four hundred twelve participants were included in analyses; 206 participants discontinued BUP-XR prematurely. Mean EQ-5D-5L scores remained stable from baseline to end of study. Statistically significant improvements from baseline to end of study were noted for the SF-36v2 mental component summary score (difference = 5.0, 95%CI: 3.5–6.5) and 7 of 8 domain scores ($P < .05$ for all comparisons); the SF-36v2 physical component summary remained stable from baseline to end of study. The TEA total score (difference = 9.3 points, 95%CI: 8.0–10.5) and 4 of 4 domain scores (difference = 2–3 points per domain) significantly improved from baseline to end of study. Significant improvements ($P < .05$ for all comparisons) on the ASI-Lite were seen for all problem areas except alcohol use from baseline to end of study. Employment rate increased 7% whereas health insurance status remained stable from baseline to end of study. Medication satisfaction measured using the MSQ was > 88% at end of study.

Conclusions: Treatment with BUP-XR monthly injections for up to 12 months in this cohort of treatment-seeking individuals with OUD led to positive PCOs and high treatment satisfaction, which correspond to personal recovery.

1. Introduction

Opioid use disorder (OUD) is associated with significant societal, physical, psychological, and economic burden (Bachhuber, Roberts, Metraux, & Montgomery, 2015; D'Onofrio et al., 2015; Fisher et al., 2014; Han et al., 2017; Stein et al., 2017). For people seeking treatment for OUD, medication-assisted treatment with buprenorphine, methadone, or naltrexone may be an option. However, very little is known about the effects of these treatments on patient-centered outcomes including health-related quality of life, satisfaction, and productivity as these are not commonly assessed in OUD treatment studies (Bray et al., 2017). Including patient-centered outcomes as a component of OUD

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management may help clinicians further support people during their recovery (Fowler Jr., Levin, & Sepucha, 2011).

RBP-6000, referred to as BUP-XR, is the first buprenorphine extended-release monthly injection, for subcutaneous use [CIII] (SUBLOCADE™, Indivior Inc) approved by the US Food and Drug Administration (FDA) (*SUBLOCADE [package insert]*, 2018). People receiving prolonged-release pharmacotherapy compared to daily oral methadone or buprenorphine may experience fewer reminders of their OUD and consequently be able to live a more normal life enabling them to travel, work, vacation, visit friends, and be spontaneous, and over time, feel more positive about themselves (Neale, Tompkins, & Strang, 2019).

Results from a randomized, double-blind trial showed that abstinence and treatment success rates were higher in participants with OUD receiving up to 6 injections of BUP-XR compared to placebo (Haight et al., 2019). In this study, participants receiving BUP-XR compared to placebo reported better health, higher medication satisfaction, increased employment, and decreased healthcare utilization over the 6-month study period (Ling et al., 2019).

The objective of the present analysis is to describe the effect of up to 12 monthly BUP-XR injections on patient-centered outcomes including health status, health-related quality of life, employment/insurance status, healthcare resource utilization, medication satisfaction, treatment effectiveness, and addiction severity. While health status, health-related quality of life, employment/insurance status, healthcare resource utilization, and medication satisfaction were also reported within the double-blind trial (Ling et al., 2019), analyses herein provide outcomes over a 12 month period in a different set of participants as compared to the 6 month follow-up within the double-blind trial. In addition, this is the first study to report on treatment effectiveness in addiction severity associated with BUP-XR.

2. Materials and methods

2.1. Study design

A multi-center, open-label, long-term clinical study (NCT02510014) was conducted evaluating up to 12 months of BUP-XR therapy in people 18 to 65 years of age who were seeking treatment for moderate or severe OUD as defined in the Diagnostic Statistical Manual 5 (DSM-5) (American Psychiatric Association, 2013). Exclusion criteria included current diagnosis, other than OUD, requiring chronic opioid treatment; current substance use disorder other than opioids, cocaine, cannabis, tobacco, or alcohol as defined by DSM-5 criteria; positive urine drug screen (UDS) at screening for cocaine or cannabis AND moderate or severe cocaine or cannabis disorder (DSM-5 criteria); or moderate or severe alcohol use disorder (DSM-5 criteria).

Participants could enroll directly into the long-term open-label study and receive up to 12 monthly BUP-XR injections or enroll following completion of the BUP-XR Phase 3, 24-week, placebo-controlled study (NCT02357901; roll-over cohort) and receive up to 6 monthly BUP-XR injections (i.e., up to 12 monthly BUP-XR injections total across both trials). Regardless of how participants entered the study, inclusion and exclusion criteria were identical. This study was conducted in accordance with International Council for Harmonization Good Clinical Practice guidelines and US Food and Drug Administration regulations governing clinical study conduct. The study protocol, amendments, informed consent form, and all other appropriate study-related information was reviewed and approved by an institutional review board. Written informed consent was obtained from study participants prior to enrollment and after procedures and possible side effects were explained.

The study consisted of a 7-day screening period, followed by a 3- to 14-day run-in period with sublingual buprenorphine/naloxone, followed by an up to 45-week BUP-XR treatment period and a 4-week follow-up period to assess whether there were any further safety signals after the last BUP-XR dose. During the run-in period, participants received sublingual buprenorphine/naloxone titrated to a maximum dose of 24 mg daily based on clinical response and physician judgment. Participants with significant withdrawal signs and symptoms (i.e., Clinical Opiate Withdrawal Scale score $>$ 12 or Opioid Craving Visual Analog Scale score $>$ 20 mm) at the end of the run-in period were withdrawn from the study, referred for appropriate treatment, and considered run-in failures. All other participants entered the treatment phase. During the BUP-XR active treatment phase, all participants received an initial 300 mg subcutaneous injection of BUP-XR. For subsequent doses, the BUP-XR dose could be reduced to 100 mg and then increased back to 300 mg based on the medical judgment of the investigator. All participants received injections of BUP-XR separated by 28 ($-2/+4$) days.

Data reported herein are for patient-centered outcome measures which were a tertiary outcome of the study. This analysis focused on participants whose first exposure to BUP-XR was during the long-term study and therefore, were eligible to receive up to 12 BUP-XR injections. Efficacy, safety, and retention outcomes will be published separately.

2.2. Patient-centered outcome measures

Instruments used to measure patient-centered outcomes included the 5-level EQ-5D (EQ-5D-5L) (Herdman et al., 2011); Short-Form-36® version 2 (SF-36v2) (Ware et al., 2008); Treatment Effectiveness Assessment (Ling, Farabee, Liepa, & Wu, 2012); Addiction Severity Index-Lite (McLellan, Luborsky, Woody, & O'Brien, 1980); stand-alone questions to assess health insurance and healthcare resource utilization (Supplemental Figure); and the Medication Satisfaction Questionnaire (Vernon et al., 2010). Patient-centered outcome measures were administered at screening, at various injection visits prior to BUP-XR administration, and at the end of study visit (Table 1).

The EQ-5D-5L is a generic and preference-weighted measure for capturing health status consisting of a health utility score and a visual analog scale score (Herdman et al., 2011). The health utility score is composed of the following 5 single-item dimensions: mobility; self-care; daily activities; pain/discomfort; and anxiety/depression. Each dimension is divided into 5 levels of severity: no, slight, moderate, severe, or extreme problems. A health utility score is calculated based on responses in the 5 dimensions and was calculated using the US crosswalk (available at https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/valuation-standard-value-sets/crosswalk-index-value-calculator/). The visual analog scale score is determined using a 20-cm scale that ranges from 0 for the worst possible health state and 100 for the best possible health state which participants indicate where they would place themselves to make a global assessment of their current state of health.

The SF-36v2 is a generic measure of health-related quality of life used to assess 8 multi-item domains (36 items in total) as well as 2 summary measures, the mental component summary and the physical component summary scores. The domain scores are transformed to a 0 to 100 scale with higher scores indicating better health; component scores are calibrated such that a score of 50 represents a US population norm.

The Treatment Effectiveness Assessment is a 4-item scale used to assess participant perception of treatment effectiveness. The Treatment Effectiveness Assessment captures patient-centered information that is meaningful and relevant to the lives of people with substance use disorders (Ling et al., 2012). Participants respond to the Treatment Effectiveness Assessment questions by providing numerical responses for 4 domains: substance use (e.g., drugs, alcohol, tobacco), health (e.g., physical, emotional health), lifestyle (e.g., housing or living situation,

Table 1
Patient-centered outcome assessment schedule.

	Screening (7 days)	Injection											End of study
		1	2	3	4	5	6	7	8	9	10	11	12	
Week		**1**	**5**	**9**	**13**	**17**	**21**	**25**	**29**	**33**	**37**	**41**	**45**	**49**
EQ-5D-5 L	X	X		X			X			X			X	X
SF-36v2	X	X		X			X			X			X	X
TEA	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ASI-Lite		X		X			X			X			X	X
Health Insurance	X	X	X	X	X	X	X	X	X	X	X	X	X	X
MSQ				X			X			X			X	X

Abbreviations: ASI, Addiction Severity Index; EQ-5D-5L, 5-Level EQ-5D; MSQ, Medication Satisfaction Questionnaire; SF-36, Short-Form-36® version 2; TEA, Treatment Effectiveness Assessment

family, employment, relationships), and community (e.g., obeying laws and becoming a responsible member of society). For each question, participants rate the extent of changes for the better from their involvement in the program on a 10-point scale, where 1 represents "not better at all" and 10 represents "very much better." The Treatment Effectiveness Assessment total score is calculated using the sum of numerical responses on the 4 Treatment Effectiveness Assessment domains and can range from 4 (no measurable improvement or worse) to 40 (significantly improved).

The Addiction Severity Index-Lite measures the severity of 7 treatment problem areas: medical, employment/support status, alcohol, drug, legal, family/social, and psychiatric (McLellan et al., 1980). A composite score is calculated for each problem area and can range from 0 to 1 with higher scores indicating more severe problems. In addition, report of any days paid for working in the last 30 days (item E11) was used to measure whether the participant was employed.

The Medication Satisfaction Questionnaire is a single-item, 7-point questionnaire that measures medication satisfaction (Vernon et al., 2010). Responses on the Medication Satisfaction Questionnaire are as follows: 1 = extremely dissatisfied, 2 = very dissatisfied, 3 = somewhat dissatisfied, 4 = neither satisfied nor dissatisfied, 5 = somewhat satisfied, 6 = very satisfied, and 7 = extremely satisfied. In addition to providing mean results, Medication Satisfaction Questionnaire scores were categorized as dissatisfied/neutral (1–4) or satisfied (5–7) to provide a simple interpretation of changes in satisfaction.

2.3. Statistical analysis

Endpoints were descriptively summarized. Consistent with the study protocol, change from baseline (i.e., first BUP-XR dose) at the end of study visit was assessed for the EQ-5D-5L index and visual analog scale scores; SF-36 domain, physical and mental component summary scores; Treatment Effectiveness Assessment total and domain scores; and Addiction Severity Index-Lite problem area scores using a mixed model for repeated measures (MMRM) controlling for baseline measurement. Baseline was defined as the value collected after the run-in period with sublingual buprenorphine/naloxone and prior to the first BUP-XR dose; end of study was week 49. All confidence intervals were 2-sided based on $\alpha = 0.05$. Unadjusted scores were also compared among complete cases only (i.e., only participants who had observed scores at every study time point) within a sensitivity analysis in order to understand potential retention effects.

3. Results

3.1. Study population

Four hundred twelve participants initiated BUP-XR treatment during the long-term clinical study and were eligible for up to 12 doses of BUP-XR. Of these, 206 (50%) discontinued BUP-XR during the treatment period, with the most common reasons for discontinuation being subject lost to follow-up (80 participants [19.4%]) and withdrawal of consent (67 participants [16.3%]). Participants were on average 38.4 years of age; 63.8% of participants were male and 71.6% were white. In terms of medication dosing, 332 (80.6%) received the 300 mg maintenance dose throughout the open-label study. Of the 80 participants who had a dose reduction from 300 mg to 100 mg, 11 participants had their dose increased back to 300 mg. Information on BUP-XR safety and efficacy during this trial will be provided in a separate publication.

3.2. Health status and health-related quality of life

Both the EQ-5D-5L index and visual analog scale scores increased from screening to baseline visits (i.e., during the sublingual buprenorphine/naloxone run-in period) and then remained stable from baseline to end of study (Fig. 1A). The least squares mean change from baseline to end of study for the EQ-5D-5L index and visual analog scale scores was not statistically different (Table 2).

Both the SF-36v2 physical and mental component summary scores increased from the screening visit to baseline (Fig. 1B). A significant improvement from baseline to end of study was noted for the mental but not the physical component summary score. All individual domain scores significantly improved from baseline to end of study except the physical functioning domain (Table 2).

3.3. Treatment effectiveness and addiction severity

Improvement was noted for all Treatment Effectiveness Assessment domain scores and the total score from screening to baseline and baseline to end of study (Fig. 1C) with significant improvement noted from baseline to end of study for all domain scores and the total score (confidence intervals did not overlap 0 for all comparisons; Table 2). For the Addiction Severity Index-Lite, significant improvements were seen for all problem areas except for alcohol use from baseline to end of study (Fig. 1D, Table 2).

3.4. Employment, health insurance, and resource utilization

The proportion of participants employed increased 7% from baseline to end of study (44.2% vs 51.2%) whereas the proportion with health insurance was stable from baseline to end of study (54.4% vs. 55.4%) (Fig. 1F). Within the 3604 person-months during which participants were followed, a total of 21 hospitalizations (78 hospital days), 140 emergency department visits, and 923 outpatient service visits were reported.

3.5. Medication satisfaction

Mean Medication Satisfaction Questionnaire scores ranged from 5.8 to 6.1 from week 9 to week 49 (Fig. 1E). At end of study, 88.8% of participants stated they were satisfied with treatment.

3.6. Sensitivity analysis for complete cases

EQ-5D index and visual analog scale, SF-36 Physical and Mental Component Summary Scores, Treatment Effectiveness Assessment and Addiction Severity Index Scores, Medication Satisfaction Questionnaire, and Health Insurance results for complete cases only remained consistent with those presented above using all observations at a given time point (Supplemental Table).

4. Discussion

Results from this study show improved or stable patient-centered outcomes and high medication satisfaction in treatment-seeking people with OUD receiving BUP-XR for up to 12 months. Although much of the benefit on patient-centered outcomes was seen during the protocol-specified stabilization phase with transmucosal buprenorphine, in general these beneficial effects were maintained throughout the study period. Additionally, this study demonstrates the feasibility of assessing outcomes other than abstinence and treatment retention in studies evaluating treatments for substance use disorders.

In participants initiating BUP-XR and receiving up to 12 monthly BUP-XR doses, patient-centered outcomes generally improved or remained stable over the open-label study period. Results from a systematic review of studies in opiate dependent individuals identified several studies that used the SF-12 or SF-36 to evaluate quality of life in patients with OUD longitudinally (De Maeyer, Vanderplasschen, & Broekaert, 2010). In general, results from this review were consistent with our results showing low quality of life at initiation of medication-assisted treatment followed by improvements in various life domains and then stabilization or slight regression in outcomes. Our results are also similar to those reported by Raisch et al. who noted improvement in health-related quality of life (SF-6D) over 16 weeks during participation in a buprenorphine pharmacokinetic study for opioid dependence and by Nosyk et al. who noted initial improvement in health-related quality of life (SF-6D) followed by a slight decrease or an increase (albeit at a diminished rate) in health-related quality of life over 24 weeks in patients receiving opioid agonist treatment for opioid dependence (Nosyk et al., 2015; Raisch et al., 2012). Results from a systematic review of studies evaluating QOL outcomes in patients with OUD who were enrolled in treatment programs highlights the need for additional research on quality of life outcomes in people with OUD disorders. Results from this review demonstrated the paucity of patient-centered data for people with OUD receiving treatment through a treatment center and noted that the majority of data are > 10 years old with few studies reporting data from the United States (Bray et al., 2017).

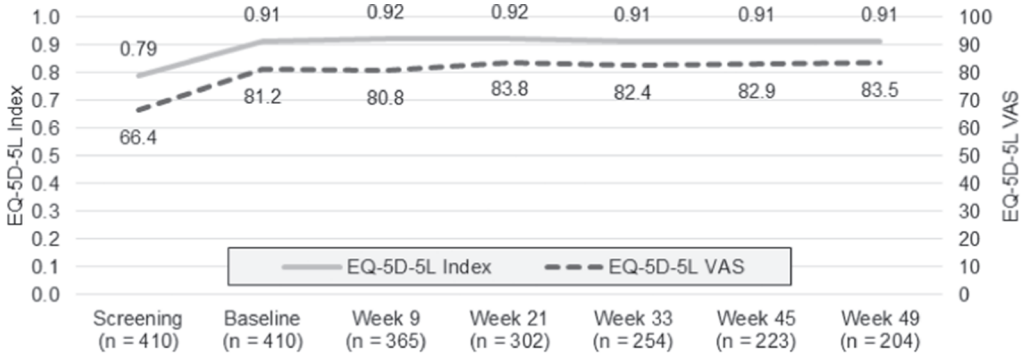
BUP-XR is the first monthly buprenorphine extended-release formulation approved in the United States and Canada for the treatment of OUD; it has also been approved for use in Australia. Numerous benefits of receiving a long-acting depot formulation compared to a once daily treatment for OUD were identified through semi-structured qualitative interviews of people using opioids and receiving treatment with methadone or buprenorphine or not on treatment and using heroin (Neale et al., 2019). Benefits of a long-acting formulation described by Neal et al. included elimination of the burden of daily OUD therapy such as the need to attend treatment services or visit a pharmacy and the ability to attend to additional activities facilitating recovery and normality such as work, vacations, travel, and visiting friends. Patients noted that a long-acting depot formulation would allow them to be more spontaneous, provide a welcomed break from the physical symptoms of withdrawal and the psychological worry that withdrawal could happen, and overall have a positive feeling. Long-acting depot formulation were also thought by patients to potentially decrease the need to commit crimes for money which would then be used to buy drugs, eliminate the embarrassment of taking their OUD treatment in front of other customers, allow them to avoid bumping into people who would try to sell or give them drugs around treatment facilities, alleviate the stress and inconvenience from having to arrange their day around attending appointments and treatment centers and enable them to forget about their opioid of choice for the duration of therapy instead of thinking about it every day.

Although this study had an open-label design, improvements were similar to those reported for participants enrolled in the Phase 3, randomized, double-blind BUP-XR study (Ling et al., 2019). In the BUP-XR double-blind study, participants randomized to BUP-XR (n = 389) compared to placebo (n = 98) following induction with transmucosal buprenorphine per dosing recommendations significantly improved on several patient-reported outcome measures including those measuring health status and health-related quality of life. Additionally, participants receiving BUP-XR reported high medication satisfaction and increases in employment (Ling et al., 2019). The similarity of benefits on patient-centered outcomes noted during both BUP-XR studies suggests that BUP-XR positively affects patient-centered outcomes in people with OUD; the current study demonstrated that those benefits remain in longer treatment windows. Moreover, rates of observed hospitalizations, emergency, and outpatient service visits were much lower than utilization observed in a claims analysis focusing on participants receiving buprenorphine medication-assisted treatment (Ronquest, Willson, Montejano, Nadipelli, & Wollschlaeger, 2018).

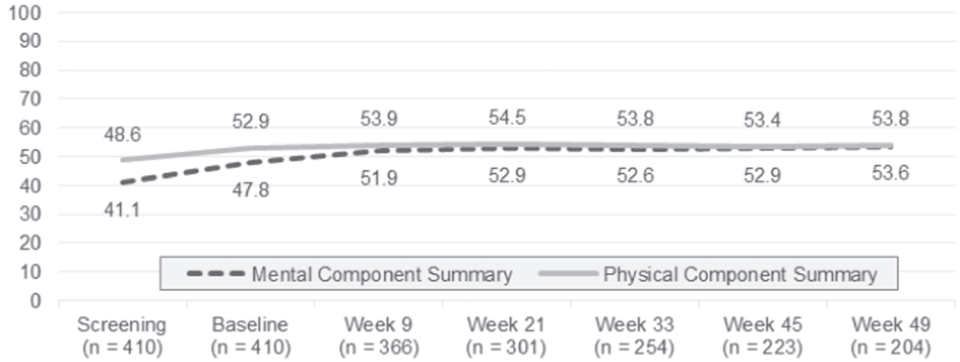
Several additional patient-centered instruments not included in the double-blind study were included in this study including the Treatment Effectiveness Assessment and the Addiction Severity Index-Lite. To our knowledge, this study is the first to report on the use of the Treatment Effectiveness Assessment in a Phase 3 clinical trial. Steady improvement on the Treatment Effectiveness Assessment was demonstrated throughout the study period and significant change from baseline to end of study noted for all Treatment Effectiveness Assessment domains and the Treatment Effectiveness Assessment total score. The Treatment Effectiveness Assessment instrument prompts participants to rate the extent of changes for the better from their involvement in the program. In the instructions given to participants in the context of this study, no specific time point was given for program involvement (e.g., before sublingual buprenorphine/naloxone run-in, before first BUP-XR injection in this study). Therefore, scores for participants likely reflect their perceived level of improvement since enrollment in this open-label clinical study, including the screening/run-in period prior to BUP-XR administration. This may provide an explanation for the increase in Treatment Effectiveness Assessment scores between screening and baseline observed at the baseline/injection 1 measurement.

Results from this study should be interpreted within the context of the following limitations. No sample size calculations were performed specifically for evaluation of patient-centered outcomes which were a tertiary outcome in this study. Therefore, the study might not have been powered to detect differences for some endpoints. Approximately half of patients withdrew from the study and did not receive 12 monthly BUP-XR injections. To contextualize this, our retention was similar to the 53% reported in a Cochran review of 11 buprenorphine maintenance therapy studies for opioid dependence (Mattick, Breen, Kimber, & Davoli, 2014). Additionally, results from a complete case analysis showed similar outcomes across time as analysis of the entire cohort. Although we reported that medication satisfaction was high ranging from 85% to 88.8% throughout the study, satisfaction was only

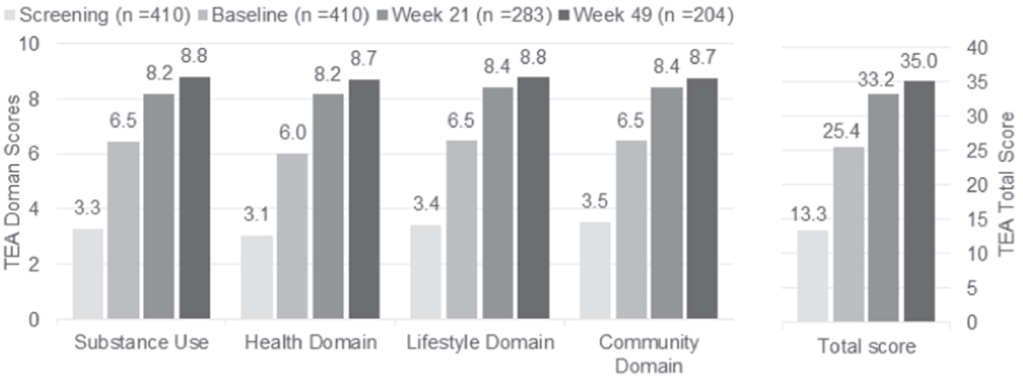
A. EQ-5D Index and VAS Scores



B. SF-36v2 Physical and Mental Component Summary Scores



C. Absolute TEA scores



D. Absolute ASI-Lite Scores

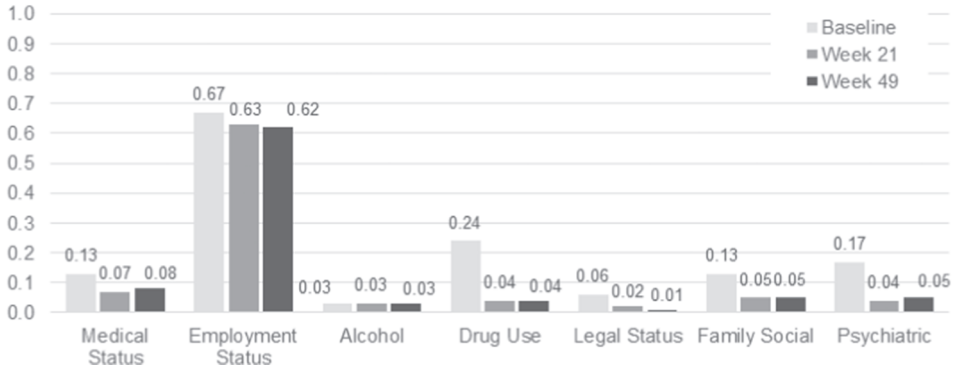


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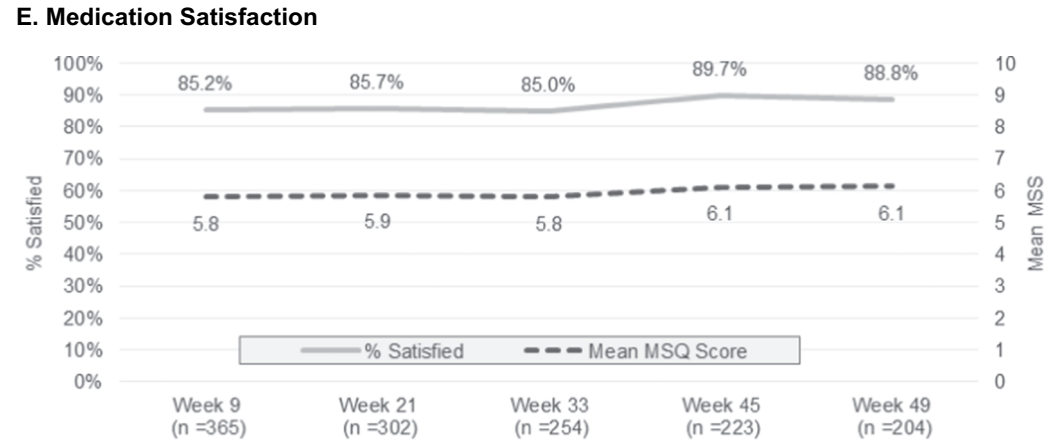
Fig. 1. Change in patient-centered outcomes over time. Fig. 1 shows the change in (A) EQ-5D Index and VAS Scores, (B) SF-36v2 physical and mental component summary scores, (C) absolute TEA domain and total scores, (D) absolute ASI-lite problem area and total score, (E) medication satisfaction, and (F) employment and health insurance. Results for the EQ-5D Index and VAS scores and the SF-36v2 PCS and MCS scores are shown from screening to end of study (i.e., week 49). The population norm for SF-36 PCS and MCS scores is 50. TEA scores are shown at screening, baseline, week 21, and end of study. ASI-Lite scores are shown for baseline, week 21, and end of study (week 49). Medication satisfaction was measured using the Medication Satisfaction Questionnaire; results are shown for weeks 9, 21, 33, 45, and end of study. Medication satisfaction was defined as somewhat satisfied (response = 5), very satisfied (response = 6), or extremely satisfied (response = 7). Employment and health insurance are presented at baseline, weeks 9, 21, 33, 45, and end of study. Abbreviations: ASI, Addiction Severity Index; EQ-5D-5L, 5-Level EQ-5D; SF-36, Short-Form-36® version 2; Treatment Effectiveness Assessment; VAS, visual analogue scale.



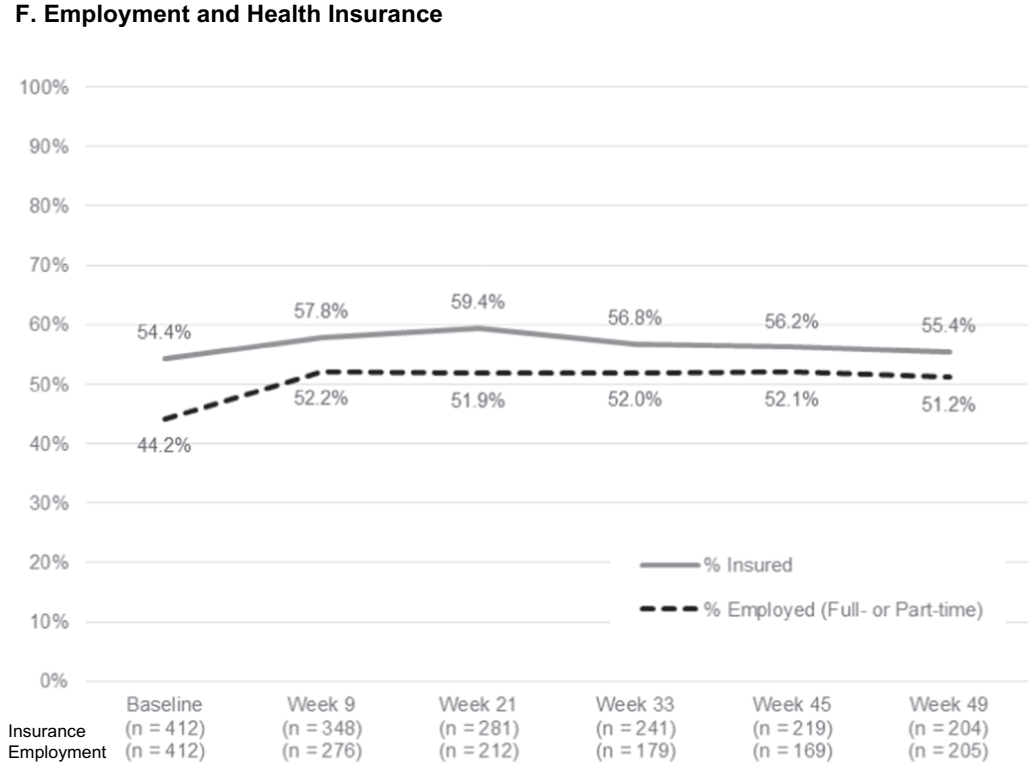


Fig. 1. (*continued*)

determined for those participants remaining in the study and does not include results for those patients who dropped out of the study. All participants within this study received BUP-XR, limiting the ability to make comparisons to patients receiving no or different treatments. Excluding people with moderate/severe alcohol use disorder or moderate or severe criteria for cocaine and/or cannabis disorder from the study may have led to less severe scores on addiction and treatment effectiveness measures.

5. Conclusions

Results from this long-term study show positive patient-centered outcomes and high treatment satisfaction for participants initiating and receiving up to 12 months of BUP-XR treatment during the open-label

Table 2
Least squares mean change from baseline (95% CI) at end of study in patient-centered outcomes.

Measure	Participants (N = 412)
EQ-5D-5L[a]	
VAS	1.64 (−1.01, 4.30)
Index	−0.01 (−0.03, 0.02)
SF-36v2[a]	
Physical component score	0.73 (−0.32, 1.79)
Mental component score	5.00 (3.46, 6.54)
Mental health	10.27 (7.35, 13.19)
Physical functioning	−1.31 (−3.95, 1.34)
Role physical	3.61 (0.27, 6.95)
Bodily pain	9.61 (5.71, 13.52)
General health	4.31 (1.30, 7.33)
Vitality	11.97 (8.63, 15.32)
Social functioning	6.75 (2.81, 10.69)
Role emotional	3.84 (0.56, 7.13)
Treatment effectiveness assessment[a]	
Substance use	2.39 (2.01, 2.77)
Health	2.54 (2.20, 2.89)
Lifestyle	2.24 (1.91, 2.58)
Community	2.17 (1.83, 2.51)
Total score	9.26 (8.01, 10.52)
ASI-lite[b]	
Medical status	−0.04 (−0.07, −0.00)
Employment status	−0.04 (−0.08, −0.01)
Alcohol use	0.00 (−0.01, 0.01)
Drug use	−0.19 (−0.21, −0.18)
Legal status	−0.05 (−0.06, −0.04)
Family and social status	−0.08 (−0.10, −0.06)
Psychiatric status	−0.11 (−0.14, −0.09)

Abbreviations: ASI, Addiction Severity Index; EQ-5D-5L, 5-Level EQ-5D; MSQ, Medication Satisfaction Questionnaire; SF-36, Short-Form-36® version 2; TEA, Treatment Effectiveness Assessment.

[a] Results from mixed models with repeated measures; positive values indicate improvement.

[b] Results from mixed models with repeated measures; negative values indicate improvement.

study, demonstrating that meaningful life changes are measurable during a person's recovery journey. Outcomes that are easily measurable during office visits can help clinicians assess life changes reflective of a person's recovery—a life style characterized not only by abstinence but also health and return to normality.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jsat.2019.11.004.

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Declaration of competing interest

WL is a consultant for Indivior Inc., Alkermes, Camurus/Braeburn, Opiant, and Titan Pharmaceutical. VRN, SML and CH are employees of and own stock in Indivior Inc. NAR was an employee of Indivior Inc. at the time of this study. CTS and YY are employees of Pharmerit International and are consultants for Indivior Inc. A family member of YY is an employee of Vertex Pharmaceuticals. VM is a clinical investigator for BUP-XR clinical trials and a consultant for Indivior Inc.

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