TOGETHER
Maine
Substance Use Disorders
Learning Community

Best Practice of the Use of Extended-Release Buprenorphine and Naltrexone

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5/4/22

Opioid
Response
Network
STR-TA/SOR-TA

Working with communities to address the opioid crisis.

- SAMHSA's State Targeted Response Technical Assistance (STR-TA) and State Opioid Response Technical Assistance (SOR-TA) grants created the *Opioid Response Network* to assist states, individuals and other organizations by providing the resources and technical assistance they need locally to address the opioid crisis .
- Technical assistance is available to support the evidence-based prevention, treatment, and recovery of opioid use disorders.

Funding for this initiative was made possible (in part) by grant 1H79TI083343 from SAMHSA. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

Working with communities to address the opioid crisis.

- The Opioid Response Network (ORN) provides local, experienced consultants in prevention, treatment and recovery to communities and organizations to help address this opioid crisis.
- The ORN accepts requests for education and training.
- Each state/territory has a designated team, led by a regional Technology Transfer Specialist (TTS), who is an expert in implementing evidence-based practices.

Contact the Opioid Response Network

- To ask questions or submit a request for technical assistance:
  - Visit www.OpioidResponseNetwork.org
  - Email orn@aaap.org
  - Call 401-270-5900

Disclosures

- John Mariani, MD, has had a financial relationship with Indivior (manufacturer of Sublocade) in the past year including payments for advisory board and speaker events
- The content of this activity may include discussion of off label or investigative drug uses.
- Trade names are used to distinguish agents with the same generic designation (e.g., extended-release buprenorphine for injection)

Objectives

- AT THE CONCLUSION OF THIS SESSION, PARTICIPANTS SHOULD BE ABLE TO:
  - Review the data supporting the use of injectable extended-release buprenorphine treatment and injectable extended-release naltrexone for opioid use disorder
  - Discuss patient selection for injectable Medications for Opioid Use Disorder (MOUD)
  - Identify special risks that fentanyl use presents and the possible role of injectable extended-release treatments.

Clinical Questions in Treating Opioid Use Disorder with Injectable Medications

- Who are the ideal patients for extended-release injectable therapy?
- When can you switch between oral formulations and extended-release injectable formulations of Medications for Opioid Use Disorder (MOUD)?
- How long to continue patients on extended-release injectable therapy?

Clinical Difficulties Inducting Fentanyl-Using Patients Onto Buprenorphine

- Standard buprenorphine induction strategies can precipitate withdrawal (Shearer, 2021)
- Withdrawal time course is more protracted, likely due to “third space” accumulation of fentanyl in adipose tissue
  - Hospitalized patients positive 8 days after admission
- More failed initial inductions
- More failed “secondary inductions”—buprenorphine maintenance patients unable to restart buprenorphine on their own

Relevant Fentanyl Pharmacology

- Fentanyl and its analogues are highly lipophilic
- High lipophilicity results in:
  - Rapid crossing of the blood-brain barrier
  - Rapid distribution to the peripheral tissue and a slow return to the central compartment
- Similar μ-opioid receptor affinity as morphine
- Definitive human studies are lacking
- Leading theory is that fentanyl is more "efficacious" at μ-opioid receptor
  - If one molecule of morphine activating one receptor is 100 units of agonism
    - Then buprenorphine is 50 units
    - And fentanyl is 150 units
  - Enormous implications for standard dosing of current opioid use disorder pharmacotherapy

(Chen,1993)(Traynor,1995)(Volpe ,2011)(McClain,1980)(Maguire,1992)(Comer 2019)

Extended-Release Naltrexone for Injection (XR-NTX)(Vivitrol™)

- Oral formulation of naltrexone approved 1984 for opioid use disorder
  - However, not shown to differentiate from placebo unless administration monitored
- XR-NTX approved in the US in 2010 for prevention of relapse to OUD following detoxification, in conjunction with psychosocial counseling
  - IM gluteal injection every 4 weeks
- XR-NTX shown to be associated with increased treatment retention, decreased relapse, and decreased cravings for opioids in outpatients and inpatients
  - (Krupitsky 2011, Nunes 2018, Lee 2018, Bisaga 2018)
- FDA prescribing instructions recommend an opioid-free duration of at least 7-10 days to avoid precipitated withdrawal
  - 5-day induction period may be feasible for outpatients (Sibai 2020)
- Cost is approximately $1400 per injection

XR-NTX Pivotal and Other Key Trials

- Pivotal trial conducted in Russia comparing XR-NTX 380 mg to placebo (n=250) (Kruptisky 2011)
  - XR-NTX superior to placebo:
    - Median proportion of weeks of confirmed abstinence 90% vs 35%
    - Self-reported opioid free days 99.2% vs 60.4%
    - Median retention: 168 days vs 96 days
- X:BOT—Comparison of XR-NTX to SL buprenorphine (n=570) (Lee 2018)
  - Fewer XR-NTX participants initiated treatment: 72% vs. 94%
  - More relapse events in XR-NTX: 65% vs. 57%; although for patients successfully inducted similar relapse events
    - Would interpret these results that XR-NTX induction is more difficult than SL Buprenorphine, but once inducted are roughly equivalent
- Outpatient XR-NTX Induction: Double-blind, placebo-controlled, study of 7 days of low and ascending doses of oral NTX or PBO used in conjunction with 3 days of tapered SL buprenorphine or placebo with plan for XR-NTX to be administered on day 8 (Bisaga 2018)
  - Induction success similar for NTX/BUP (46%), NTX/PBO-B (40.5%) vs. PBO-N/PBO-B (46%)
  - Use of ascending naltrexone or buprenorphine does not assist in XR-NTX induction success
    - also (Comer 2020)

XR-NTX for Injection (Vivitrol)

- Advantages
  - Injectable formulation ensures compliance for 1 month at a time
  - No physical dependence on therapeutic agent (can also be a disadvantage)
  - Provides some protection against fatal overdose (Ma 2019)
    - Although, inconsistent evidence (Morgan 2019)
    - Probably less so in fentanyl-era
- Disadvantages
  - Blocking effects may start to decay closer to 3 weeks
  - Induction is difficult, need opioid-free period of abstinence, which is particularly difficult to accomplish as an outpatient
  - Lowering of opioid tolerance MAY increase risk of opioid overdose when non-compliant or treatment discontinued (Saucier 2018)
  - Expensive

Extended-Release Buprenorphine for Injection (BXR)

- Sublingual formulation of buprenorphine approved in US in 2002 for opioid use disorder
  - Very effective and adopted widely
  - Main disadvantages are noncompliance and diversion
- 1st BXR approved in the US in 2017 (Sublocade™) for the treatment of moderate-severe OUD after stabilization on SL buprenorphine for 1 week (available since 2019)
  - Two available strengths, 300 mg and 100 mg
  - SC abdominal injection every 4 weeks
  - Cost is approximately $1700 per injection
  - Rapid induction to Sublocade may be safe and feasible (Mariani 2020, Mariani 2021)
- 2nd BXR approved in the US in 2018 (Brixadi™)
  - Not yet available first due to 3-year exclusivity granted to Sublocade, then FDA inspection of manufacturing facility, now has resubmitted to FDA, last update 12/21 with no guidance on when drug will be available commercially
  - Weekly (8, 16, 24 or 32 mg) or monthly (64, 96, 128 or 160 mg) used in pivotal trial, all of those strengths, except the 160 mg monthly, are planned to be available commercially

Sublocade Pivotal Trial

- Placebo-controlled 3-arm trial (n = 504)(Haight 2019) comparing:
  - BUP-XR 300 mg/100 mg (2 x 300 then 4 x 100 mg)
  - BUP-XR 300 mg/300 mg (6 x 300 mg)
  - PBO
- Two week Open-Label run up with buprenorphine film
  - 8-24 mg SL daily
- Mean Participants % Abstinence

  (defined as percentage of negative urine samples and self-report from weeks 5 to week 24)
  - BUP-XR 300 mg/300 mg (41.3%)
  - BUP-XR 300 mg/100 mg (42.7%)
  - PBO (5 %)
- Labelling instructions recommends 7-days SL buprenorphine of at least 8 mg daily before injection
- Retention rates for Bup-XR at 12 months 50.6% (Andorn 2020)

Sublocade Pharmacokinetics

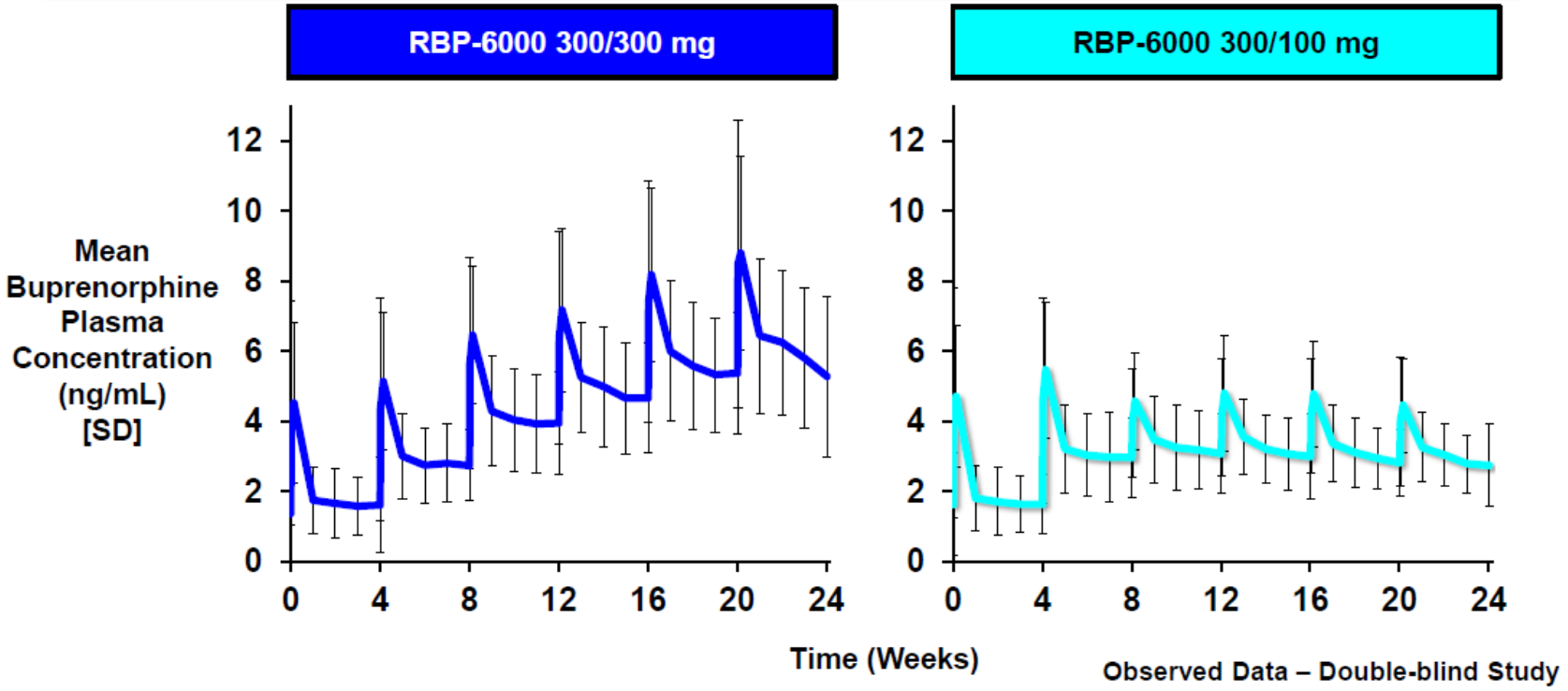
Table 7 Comparison of Steady-state Buprenorphine Plasma Exposure Between Daily Transmucosal Buprenorphine and Once Monthly SUBLOCADE at Trough (C_{trough}), Average (C_{avg}) and Peak (C_{max}) Levels (Geometric Mean (CV%))

Pharmacokinetic parameters	Transmucosal Buprenorphine				SUBLOCADE	
	8 mg	12 mg	16 mg	24 mg	100 mg	300 mg
$C_{avg,ss}$ (ng/mL)	1.37 (40)	1.79 (40)	2.16 (40)	2.84 (40)	2.87 (32)	6.32 (32)
$C_{max,ss}$ (ng/mL)	4.27 (45)	5.60 (45)	6.77 (45)	8.86 (45)	5.10 (33)	11.81 (35)
$C_{trough,ss}$ (ng/mL)	0.66 (63)	0.87 (63)	1.04 (61)	1.37 (62)	2.46 (40)	5.47 (39)

(Sublocade FDA Prescribing Information)

Sublocade PK in Phase 3 Double-Blind Study

RBP-6000 PK in Phase 3 Double-Blind Study



(https://www.fda.gov/media/108382/download)

300/300 group received Sublocade 300 mg every month
300/100 group received Sublocade 300 mg for two months followed by 100 mg monthly

Brixadi Pivotal Trial

- Double-dummy design comparing injectable vs. SL buprenorphine formulations (n= 428)
  - Non-inferiority as primary outcome was met
- Phase 1: 12 weeks weekly injection
- Phase 2: 12 weeks monthly injection
- On day of randomization, received 4 mg SL buprenorphine, followed by randomization to either SL or injection treatment arms
  - 1st Injection weekly injection equivalent to 8 mg SL
  - 2nd injection on day 3-4 equivalent to 4 mg SL
- The response rates were (14.4%) for the SL-BPN/NX group and (17.4%) for the Brixadi group ($P < .001$)
  - Response rate defined as abstinence at pre-defined study points
- The proportion of opioid-negative urine samples was (28.4%) for the SL-BPN/NX group and (35.1%) for the Brixadi group, a 6.7% difference ($P < .001$)

(Lofwall, 2018)

Comparison of Sublocade and Brixadi

- No direct efficacy comparisons available
  - Brixadi was “non-inferior” to SL buprenorphine
  - Sublocade was superior to placebo
- Brixadi available in weekly and monthly formulations in several formulations
  - Weekly (8, 16, 24 or 32 mg) or monthly (64, 96, 128 or 160 mg)
    - Good dosing flexibility
    - Unclear how weekly injection is an advantage
- Sublocade 300 mg and 100 mg monthly formulations available
  - Would be useful to have 200 mg dose, was studied, unclear why not produced commercially
- Great to have these options available, but much to be learned
  - Should all OUD patients being treated with buprenorphine be started on an injectable product?
  - No controlled studies on subgroups who would likely benefit from injectable formulation vs SL
- Many research questions remain to be answered to guide clinical decision making

Pilot Clinical Trial: Sublocade for HPSO (Highly Potent Synthetic Opioids)

- Difficulty with buprenorphine and XR-NTX inductions in patients positive for HPSO
- Hypothesis that BXR for injection would have utility for HPSO patients
- Open-label uncontrolled pilot study to demonstrate feasibility and have flexibility to develop optimal induction method
- 7-day stabilization period described in labelling was thought to be unnecessary
  - Registry trial had 2 weeks open-label run up on SL buprenorphine prior to randomization
  - What about patients who can't tolerate SL induction?

Phase 1 (2- or 3-day induction)

Subject	Day 1	Day 2	Day 3	Day 4	Current Status
001	• COWS = 10 at start of induction • BUP-SL = 24 mg	• BUP-SL 16 mg • BXR 300 mg injection	• COWS = 7	• COWS = 4	• Received 3 BXR injections • Completed trial • No opioid use since day prior to start of induction
003	• COWS = 10 at start of induction • BUP-SL = 10 mg	• BUP-SL = 24 mg	• BUP-SL 16 mg • BXR 300 mg injection	• COWS = 0	• Received 3 BXR injections • Completed trial • No opioid use since receiving 1st BXR injection
004	• COWS = 16 at start of induction • BUP-SL = 24 mg	• BUP-SL 16 mg • BXR 300 mg injection	• COWS = 0	• COWS = 0	• Received 3 BXR injections • Completed trial • No heroin use since second BXR injection
005	• COWS = 12 at start of induction • BUP-SL = 24 mg	• BUP-SL 8 mg	• BUP-SL 16 mg • BXR 300 mg injection	• COWS = 2	• Received 3 BXR injections • Completed trial • Intermittent heroin use after 3rd injection
006	• COWS = 10 at start of induction • BUP-SL = 24 mg	• BUP-SL 8 mg	• BUP-SL 16 mg • BXR 300 MG injection	• COWS = 0	• Received 1 BXR injection; refused 2nd injection • Retained in trial 5 weeks • No heroin use after 1st injection

(Mariani, 2020)

Phase 2 (One Day Induction)

Participant	Day 1	Day 2	Day 3	Day 4	Clinical Status
#1 41 y/o Hispanic Male Intravenous heroin 13 bags/day Utox: +Fentanyl/+Morphine	• COWS = 11 at the start of the induction • Total BUP-SL = 24 mg in divided doses • BXR 300 mg injection • COWS = 9 at the end of the induction	• Missed Visit	• COWS = 0	• COWS = 1	• Received 3 BXR injections • Completed Trial • 4 days heroin use in first 28 days post-induction • 5 days heroin use in 28 day period after 2nd injection • 4 days heroin use in 28 day period after 3rd injection • Longest continuous heroin using period was 2 days
#2 33 y/o White Male Intranasal heroin 15 bags/day Utox: +Fentanyl/+Morphine	• COWS = 9 at the start of the induction • Total BUP-SL = 24 mg in divided doses • BXR 300 mg injection • COWS = 4 at the end of the induction	• COWS = 2	• COWS = 0	• COWS = 2	• Received 3 BXR injections • Completed Trial • No heroin use after receiving 1st BXR injection for remainder of the study
#03 26 y/o White Male Intravenous heroin 15 bags/day Utox: +Fentanyl/+Morphine	• COWS = 8 at the start of the induction • Total BUP-SL = 24 mg in divided doses • BXR 300 mg injection • COWS = 11 at the end of the induction	• COWS = 7	• COWS = 5	• COWS = 0	• Received 3 BXR injections • Completed Trial • 2 days heroin use in first 28 days post-induction • Longest heroin continuous using period was 1 day • No heroin use after receiving 2nd BXR injection for the remainder of the study
#4 29 y/o White Female Intravenous heroin 8 bags/day Utox: +Fentanyl/+Morphine	• COWS = 18 at the start of the induction • Total BUP-SL = 24 mg in divided doses • BXR 300 mg injection • COWS = 9 at the end of the induction	• COWS = 3	• Missed Visit	• COWS = 7	• Received 3 BXR injections • Completed Trial • 14 days heroin use in first 28 days post-induction • 8 days heroin use in 28 day period after 2nd injection • 3 days heroin use in 28 day period after 3rd injection • Longest continuous heroin using period was 5 days
#5 40 y/o Black Male Intranasal heroin 8 bags/day Utox: +Fentanyl/+Morphine	• COWS = 17 at the start of the induction • Total BUP-SL = 24 mg in divided doses • BXR 300 mg injection • COWS = 15 at the end of the induction	• COWS = 0	• COWS = 0	• Missed Visit	• Received 3 BXR injections • Completed Trial • 9 days heroin use in first 28 days post-induction • 7 days heroin use in 28 day period after 2nd injection • Longest heroin continuous period was 3 days • No heroin use after 3rd injection

(Mariani, 2021)

Open-Label Induction Study with 5-month extension

Pools an open-label induction study and 5-month extension study

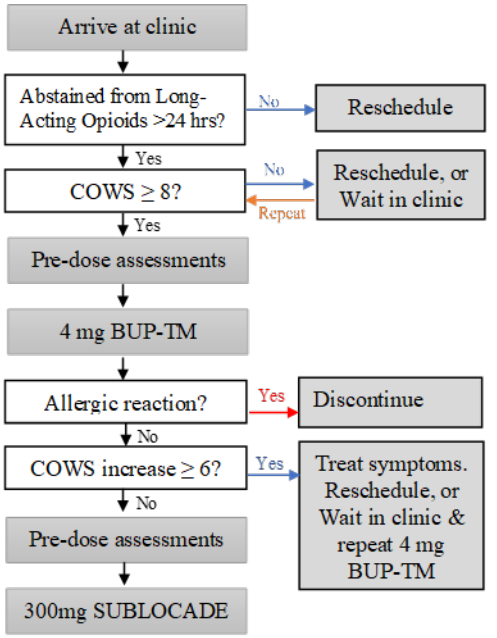
Key Inclusion/Exclusion Criteria

- ≥18 years of age
- Documented history of moderate or severe OUD as defined by Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5)
- Seeking buprenorphine-assisted treatment for OUD
- Abstained from short-acting opioids for at least 6 hours and long-acting opioids for 24 hours before arriving at the clinic on the morning of Day 1

FEN+ subjects were identified via positive urine screen for fentanyl at the Screening visit

Endpoints

- COWS scores
- Precipitated withdrawal
- Treatment retention
- Abstinence by urine drug screen



BUP=buprenorphine; COWS=Clinical Opiate Withdrawal Scale; TM=transmucosal

Wiest, et. al. Initiating Monthly Buprenorphine Injection After Single Dose of Sublingual Buprenorphine. #W102; Presented at College on Problems of Drug Dependence (CPDD); June 23, 2021.

Rapid Initiation of XR-Buprenorphine in Fentanyl Using Patients

Subject Disposition and Subject Characteristics

- 20 of 26 enrolled subjects were fentanyl-positive by urine drug screen but only 5 self-reported use of fentanyl.
- FEN+ subjects
  - 20 received BUP-TM
  - 18 received BUP-XR injection
  - 14 elected to receive a second injection
  - 11 subjects received all 6 injections
- FEN- subjects
  - 6 received BUP-TM followed by BUP-XR
  - 3 elected to receive a second injection
  - 1 subject received all 6 injections

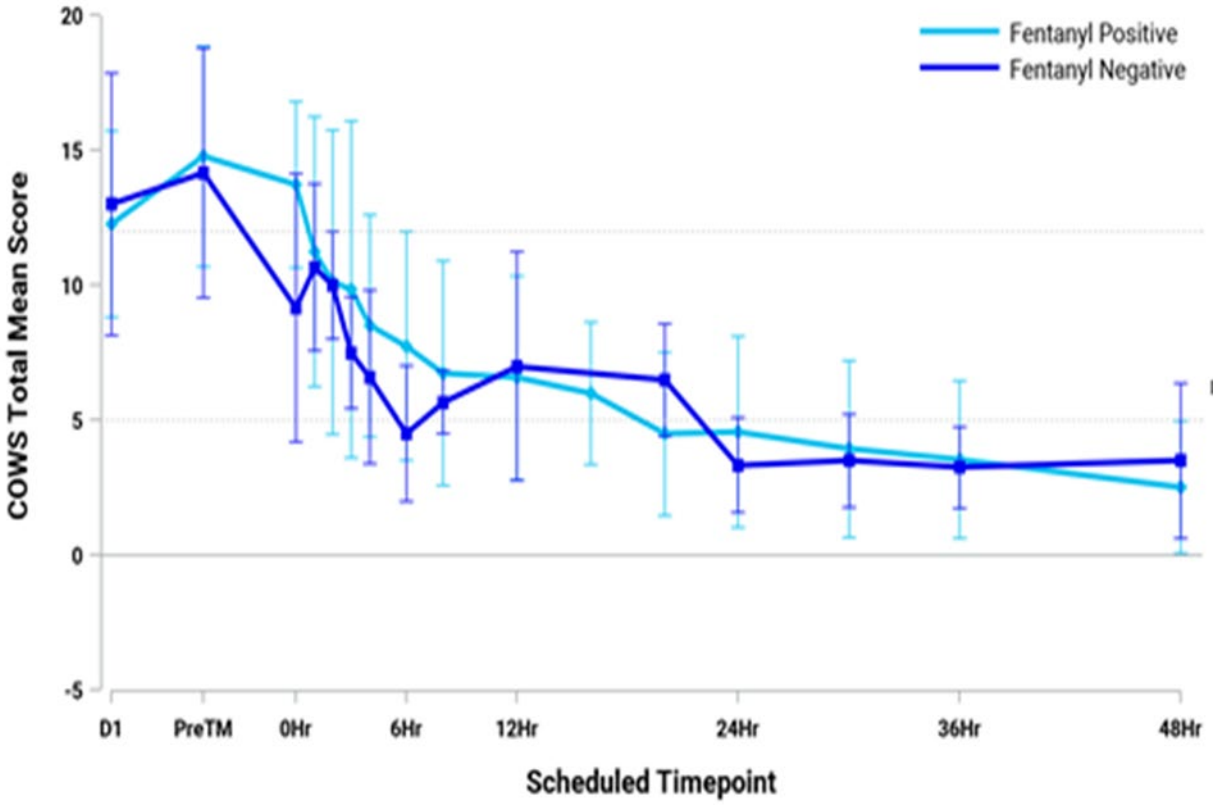
Parameter 88	FEN+ (N=18)	FEN- (N=6)
Age (Years)	43.6±12.7	29.3±10.11
Sex		
Male	8 (44.4%)	4 (66.7%)
Female	10 (55.6%)	2 (33.3%)
Race		
Black/African American	6 (33.3%)	3 (50.0%)
White/Caucasian	11 (61.1%)	2 (33.3%)
Other	1 (5.6%)	1 (16.7%)
Ethnicity		
Not Hispanic or Latino	17 (94.4%)	5 (83.3%)
Not Reported	1 (5.6%)	1 (16.7%)
BMI (kg/m^2)	23.04±4.49	21.25±2.10
Opioid Use		
Opioids – Lifetime Use (years)	14.8±14.9	11.11±8.8
Opioids – Last 30 days (days)	30.0±0.0	25.5±7.0
Opioids – Intravenous Route	6 (33.3%)	0 (0%)
Day 1 Use by Self-Report		
Opioids	18 (100%)	2 (33.3%)
Fentanyl	5 (27.8%)	0 (0%)
Oxycodone	0 (0%)	4 (66.7%)

Mariani, et. al. Rapid Initiation of Extended Release Buprenorphine in Patients using Fentanyl and Fentanyl Analogs. Presenting at Canadian Society of Addiction Medicine - La Société Médicale Canadienne sur L'Addiction (CSAM-SMCA); October 21-23, 2021.

Rapid Initiation of XR-Buprenorphine in Fentanyl Using Patients

- COWS scores in FEN+ subjects decreased from a pre-BUP-XR baseline of 13.7±3.1 to 7.8±4.2 at 6h and to 4.6±3.5 at 24h
- 2 FEN+ subjects experienced precipitated withdrawal during initiation, but still completed all 6 injections

COWS Scores

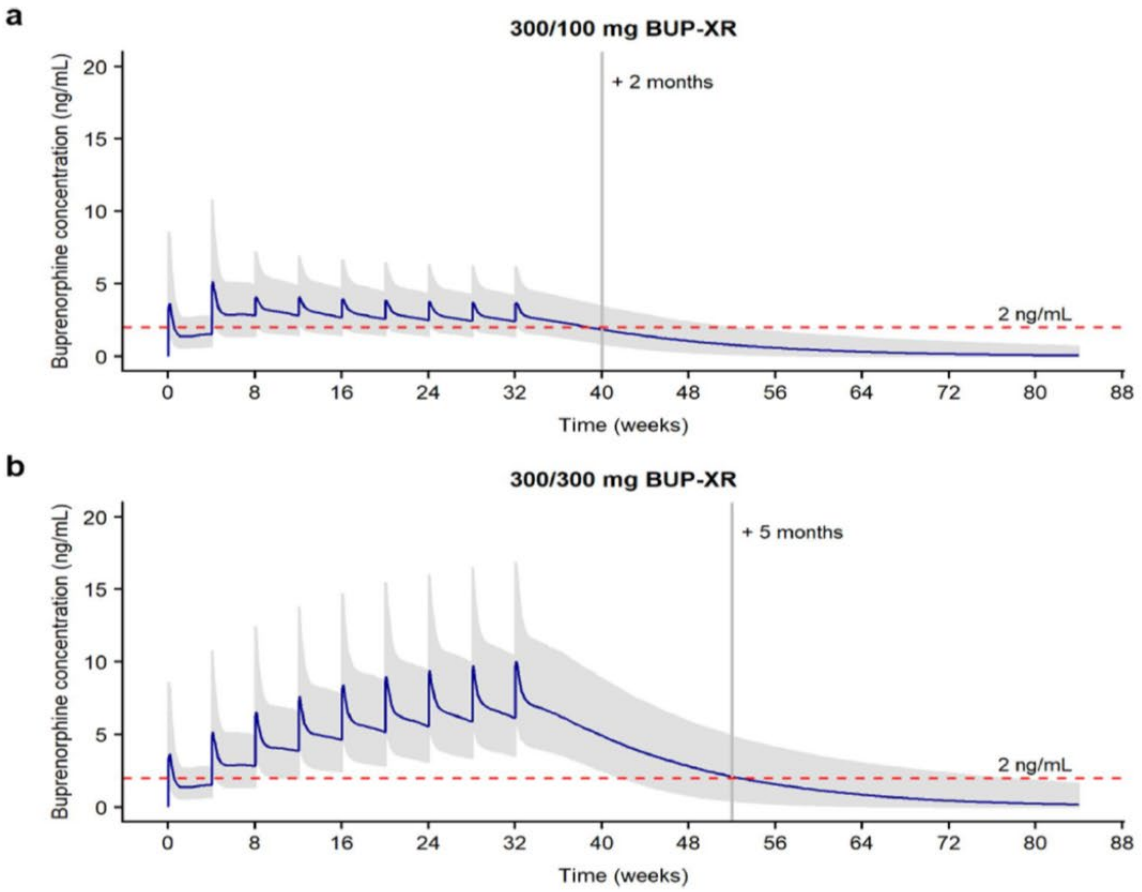


D1= Day 1 Check-in, PreTM=Pre TM Buprenorphine, 0hr=time of injection

Mariani, et. al. Rapid Initiation of Extended Release Buprenorphine in Patients using Fentanyl and Fentanyl Analogs. Presenting at Canadian Society of Addiction Medicine - La Société Médicale Canadienne sur L'Addiction (CSAM-SMCA); October 21-23, 2021.

Sublocade Discontinuation Pharmacokinetics

Fig. 6 Predicted decrease in buprenorphine plasma concentrations for BUP-XR dosing regimens following treatment interruption. **a** 300/100-mg dosing regimen 2; **b** 300/300-mg dosing regimen. Blue solid lines: median of the simulated data; gray shaded areas: 90% prediction intervals of simulated data. A total of nine subcutaneous injections were simulated in 5000 subjects. The horizontal red dashed line indicates the 2-ng/mL minimum concentration required for opioid blockade, as established from modeling and simulation and confirmed by clinical data (Nasser et al. [18])



(Jones, 2020)

Extended-Release Buprenorphine Injection to Discontinue Sublingual Buprenorphine

- Tapering off sublingual buprenorphine can be challenging because of intolerable withdrawal symptoms
- A single dose of extended-release buprenorphine may facilitate discontinuation of buprenorphine
- Case series of 3 successful transitions using a single Sublocade 100 mg injection
- 1 case transition from 4 mg SL to 100 mg Sublocade
- 1 case transition from 2 mg SL to 100 mg Sublocade
- 1 case transition from 6 mg SL to 100 mg Sublocade
- Limited evidence, but promising concept

(Ritvo, 2021)

Patient Selection for Extended-Release Injectable MOUD

- Key issue is that the ER-injectable medications reliably provide effective medication for a prolonged period of time, which should be an advantage for non or partially compliant patients and eliminate the risk of diversion
  - However, there are limited clinical trial data comparing oral/sublingual formulations to ER-injectable formulations
- Important questions about which patients benefit differentially from ER-injectable formulations
- And no data comparing the different ER-injectable formulations
- Additional important clinical factor is the emergence of fentanyl analogs as the leading cause of overdose in the US
- Almost all clinical trial data was collected in the pre-fentanyl era, and how to best treat fentanyl using patients is mostly unknown.
- Limited data of ER-Bup use in pregnancy
  - Case series of 3 patients (Cleary 2020)
  - Potential concern over safety of non-buprenorphine components of ER-Bup injection

Injectable Naltrexone (XR-NTX) vs. Injectable Buprenorphine (BXR)

- No clinical trial data, but clinical experience suggests….
- Induction (favors BXR)
- Overdose Protection (likely favors BXR)
- Availability (at present likely favors XR-NTX)
  - More clinicians familiar with XR-NTX
  - Easier insurance approval
- Fentanyl/heroin users (likely favors BXR)
- Who is ideal XR-NTX patient?
  - Prescription painkiller user with low opioid tolerance
- Who is ideal BXR patient?
  - Sublingual buprenorphine treatment failure
  - Fentanyl/heroin users (regardless of treatment history)

Role for Injectable XR Buprenorphine in 2022

- Advantages
  - All the pharmacodynamic advantages of SL buprenorphine
  - Assured compliance for 4-6 weeks
  - Clinical effects >5 weeks
  - Maintains at higher serum level than patients would take sublingually
  - Induction may be easier than sublingual with fentanyl users
  - Diversion/compliance special populations (e.g., criminal justice system)
- Disadvantages
  - Cost
  - Accessibility (insurance prior authorization, shipping)
  - Nodules are noticeable on abdomen
- Two Different Preparations
  - Sublocade (available now)
  - Brixadi (available in 2022?)

Transitions Between ER-Injectable MOUD and Other Therapies

- SL buprenorphine to BXR is very easy, can be done at any time
- SL buprenorphine or methadone to XR-NTX requires complete opioid free washout
- Methadone to BXR (or SL-BUP) requires reduction in dose (< 20-30 mg) and 48 hour spacing of last dose of methadone and first dose of buprenorphine
- BXR to XR-NTX is difficult as BXR continues to release trace amounts of buprenorphine for several months
- XR-NTX to BXR (or SL-BUP) can be accomplished 3-4 weeks after XR-NTX injection

How Long to Continue With ER-Injectable Treatment?

- Most clinical trials are 6 months, rarely 18 months
- Longer treatment with MOUD in general (> 1 year vs. < 1 year) is associated with reduced risk of fatal overdose (Ma 2019)
- Limited clinical trial data to guide decisions, but we can assume
  - Longer length of treatment is likely to be better
  - Ensuring the medication is in the patient is better than not for riskier cases
- Ultimately, length of treatment is going to be a clinical decision that takes the patient's particular risk profile into account
  - The more risk factors for fatal overdose (IV route, heroin/fentanyl, past hx of overdose), the stronger argument for longer duration of treatment
  - And probably XR-Injection for higher risk cases
- At 1-year on Sublocade, medication "satisfaction" > 88% (Ling 2020)

Regulatory, Insurance, Logistical Issues

- Sublocade and Brixadi are controlled substances, requires ordering physician to have DEA-waiver (X-Number) and to complete a REMS (Risk Evaluation and Mitigation Strategies) training, and require locked storage
  - Sublocade requires refrigeration
  - Brixadi does NOT require refrigeration
- XR-Naltrexone is NOT a controlled substance, does NOT require DEA waiver or REMS training, does NOT require locked storage
  - Naltrexone does require refrigeration
- Insurance payers almost always require prior authorization process, usually through medical benefit
- Medication is shipped from a specialty pharmacy

Injection Procedures

- Sublocade and Brixadi are subcutaneous injections to abdomen
  - Brief burning sensation after injection
  - Gel forms a solid lump which is noticeable on thin patients
- XR-naltrexone is an intramuscular injection (4 cc) into the upper-outer gluteal region
- Any injectable medication has the potential for injection site reactions/complications

Injection Instruction Videos

- Sublocade
  - https://www.sublocadehcp.com/resources
- Vivitrol
  - https://www.vivitrolhcp.com/dosing-and-administration

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