Adapting Pharmacologic Treatment to the Evolving Face of Opioid Use Disorder

Christine Rarrick, PharmD, MBA, BCPS, BCPPClinical Pharmacy Specialist—Psychiatry MUSC Health

Disclosures & CME Credit

• Neither the case presenter not the didactic presenter have conflicts of interest

• Off label use of medications may be discussed

• Project ECHO is supported through funding from the SC State Targeted Response Grant (MUSC-STR-17) through the 21st Century Cures Act (TI080221).

TheMedicalUniversityofSouthCarolinadesignatesthisliveactivityforamaximumof1.0AMAPRACategory1Credit(s)™.Physiciansshouldclaimonlythecreditcommensuratewiththeextentoftheirparticipationintheactivity.

TheMedicalUniversityofSouthCarolinaisaccreditedbytheAccreditationCouncilforContinuingMedicalEducation(ACCME)toprovidecontinuingmedicaleducationforphysicians.

InaccordancewiththeACCMEEssentials&Standards,anyoneinvolvedinplanningorpresentingthiseducationalactivitywillberequiredtodiscloseanyrelevantfinancialrelationshipswithcommercialinterestsinthehealthcareindustry.Thisinformationislistedbelow.Speakerswhoincorporateinformationaboutoff-labelorinvestigationaluseofdrugsordeviceswillbeaskedtodisclosethatinformationatthebeginningoftheirpresentation.

Medication Assisted Treatment (MAT) Options

Pharmacologic Options

Needle

• Methadone

• Naltrexone

Long-acting intramuscular injection (Vivitrol®)• Buprenorphine

Sublingual products (Suboxone®, Zubsolv®)

Subdermal Implant (Probuphine®)

Long-acting subcutaneous injection

RBP-6000 (Sublocade®)

CAM2038 (BrixadiTM) Benefits of Long-Acting Injectables (LAI)

https://www.cdc.gov/mmwr/volumes/65/wr/mm6541a5.htm?s_cid=mm6541a5_w

Naltrexone

Vivitrol®

Product Information

Naltrexone: opioid antagonist with high μ-receptor affinity

Reversible inhibitionMinimizes euphoric effects if opioids are usedReduces opioid cravings

No CYP involvementLong-acting injectable: intramuscular administration every 4 weeks

380-mg solution in microsphere formulationGluteal injection site

Elimination half-life 5 to 10 days post injectionVivitrol® [Package Insert]

Evidence for Use

Design

Open-label, active-comparison, multicenter, 24-week RCT

Interventions

Extended-release naltrexone (XR-NTX)

Sublingual buprenorphine (BUP-NX)

PrimaryEndpoint

Rate of relapse free survival

SecondaryEndpoints

Failure to initiate treatment

Opioid use during treatment

Opioid craving

Safety

InclusionCriteria

18 years or older

DSM5 criteria for OUD

Opioid use within previous 30 days

ExclusionCriteria

Serious medical or mental health disorders

Comorbid substance use disorders

PatientCharacteristics

570 patients

Average age 33 years

Majority intravenous heroin use

Lancet2018;391:309-18

Outcomes

• Similar completion rate

62% XR-NTX vs 67% BUP-NX• Significantly higher drop out during XR-NTX initiation

Early randomization reduced successful initiation• Overall lower relapse with BUP-NX

HR 1.36 (95% CI 1.1 to 1.68)

Non-significant when controlling for successful imitation• Both treatments reduced craving

• Minimal adverse eventsRBP-6000

Sublocade®

Product Information

Buprenorphine: partial opioid agonist with high μ-receptor affinity

Reduces withdrawal & cravings

CYP3A4 metabolism

80 to 95% μ-receptors are bound at a dose of 16 mg sublinguallyRBP-6000: subcutaneous injection administered every 4 weeks

Atrigel®forms polymer on contact with bodily fluids ¯

Risk of thrombosis if injected into vein

Forms palpable deposit in abdominal tissue that degrade over time

REMS required for pharmacies & providersPharmacokinetic modeling suggests 200 mg achieves ≥70% receptor blockade

Recommend two 300-mg loading doses, followed by 100 mg monthlyBuprenorphine [Package Insert]

Sublocade® [Package Insert]

Clin Pharmacokinet2014;53:813-24

Evidence for Use

Design

Double-blind, placebo-controlled, multicenter, 24-week RCT

Active Interventions

6 once-monthly 300 mg injections (n=203)

2 once-monthly 300 mg injections followed by four 100 mg injections (n=201)

Primary Endpoint

Negative UDS and self-reports of illicit opioid use

Secondary Endpoints

Rate of treatment success (≥80% negative UDS during weeks 5-24)

Reported opioid cravings

Adverse Events

Inclusion Criteria

DSM5 criteria for moderate to severe OUD for at least 3 months

Treatment seeking

BMI ≥ 18 and ≤ 35 kg/m2

Exclusion Criteria

Moderate to severe cocaine, cannabis, or alcohol use disorder

Patient Characteristics

504 patients randomized

Average age 40 years

40% injecting opioids

https://clinicaltrials.gov/ct2/show/NCT02357901

• Improved treatment retention

• Reduced self-reported opioid use, positive UDS, & self-reported opioid craving

• Clinical liver enzyme elevation: 12.4% of higher dose buprenorphine

• Gastrointestinal side effects most commonly reported

• 25-week extension study lost 42 of participants

1 patient dropped out due to adverse event

29 withdrew or lost to follow-upSublocade® [Package Insert]

https://clinicaltrials.gov/ct2/show/NCT02357901

https://clinicaltrials.gov/ct2/show/results/NCT02896296?term=rbp6000&rank=3

CAM2038

BrixadiTM

Product Information

Weekly and monthly formulations available

Pharmacokinetic equivalency• FluidCrystal®depot forms a crystalline gel for slow dissolution

Recommended administration in abdomen, arm, thigh, or buttock

Evidence for Use

Design

Double-blind, double-dummy, active-controlled, multicenter, 24-week RCT

Active Interventions

12 weekly subcutaneous (SQ) injections followed by 3 monthly injections (n=213)

Sublingual (SL) buprenorphine/naloxone (n=215)

Primary Endpoint

Percentage negative UDS

Responder rate defined as no opiate use at specified time points

Secondary Endpoints

Study retention

“Need-to-use” visual analog scale

Opioid withdrawal

Inclusion Criteria

Moderate to severe OUD

Exclusion Criteria

Pharmacologic therapy for OUD within 60 days

Recent or current suicidal ideation

Patient Characteristics

428 participants randomized

Predominantly men, average age 38.4 years

Average opiate use 4 years, predominantly using heroin

JAMA IntMed2018; 178(6):764-73JAMA IntMed2018; 178(6):764-73

• No difference in 28-week study retention

• No difference in withdrawal symptoms

• No difference in reported cravings

• Injection-site pain most commonly reportedJAMA IntMed2018; 178(6):764-73

OutcomesEvidence for Use–Extension Study

Design

Open-label, multicenter, 48-week study

Active Interventions

Weekly or monthly SQ buprenorphine

Primary Endpoint

Long-term safety and tolerability

Secondary Endpoints

Illicit opioid use

Retention in treatment

Inclusion Criteria

Moderate to severe OUD

Exclusion Criteria

Comorbid substance use disorder

Recent or current suicidal ideation

Patient Characteristics

227 participants randomized

Predominantly men, average age 41.4 years

Average opiate use 14.8 years, predominantly using heroin

Addiction, 2019; 114(8):1416-1426Addiction, 2019; 114(8):1416-1426

Dosing Results

Mean duration of exposure: 39.1 weeks (SD 16.2) N= 227

Weekly

75 (33%)

25 (67.6%)

50 (26.3%)

Monthly

77 (33.9%)

N/A

77 (40.5%)

Combination

75 (33%)

12 (32.4%)

63 (33.2%)

Addiction, 2019; 114(8):1416-1426

Safety and Efficacy Endpoint

• Treatment emergent adverse events (TEADEs):

143 (63%) reported at least one TEADE

60 of these (26.4%) considered to be drug related

Pain, swelling/erythema most common (19.8%)

Headache 7.9%

Nausea 7.0%

Vomiting 5.3%• Retention

188 (82.8%) completing 24 weeks

167 (73.6%) completing treatment periodAddiction, 2019; 114(8):1416-1426

Opioid Negative UDSReferences

American Psychiatric Association 2013.Diagnostic and statistical manual of mental disorders(5th ed.). Arlington, VA: American Psychiatric Publishing.

Buprenorphine [Package Insert]

Cicero TJ et al. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. JAMA Psychiatry 2014;71(7):821-6

Frost M, Bailey GJ, LintzerisN, et al. Long-term safety of weekly and monthly subcutaneous buprenorphine

https://www.cdc.gov/mmwr/volumes/65/wr/mm6541a5.htm?s_cid=mm6541a5_w

https://clinicaltrials.gov/ct2/show/NCT02357901

https://clinicaltrials.gov/ct2/results?cond=&term=buprenorphine&cntry=&state=&city=&dist

http://justplainkillers.com/data/

KapmanK et al. American Society of Addiction Medicine (ASAM): National practice guideline for the use of medications in the treatmentof addiction involving opioid use. J Addict Med 2015;9(5):358-67

Lee J, et al. Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial. Lancet.2018;391:309-18.

Nasser, et al. A population pharmacokinetic and pharmacodynamic modeling approach to support clinical development of RBP-6000, anew, subcutaneously injectable, long-acting, sustained-release formulation of buprenorphine, for the treatment of opioid dependence. Clinical Pharmacokinet.2014;52:813-24.

Sublocade[Package Insert]

Vivitrol [Package Insert]

MUSC designates this live activity for a maximum of 1.0AMA PRA Category 1 Credit(s)™

MUSC will award 0.1 CEUs for this activity (1 contact hour = 0.1 CEU)

CMEs and CEUs1stand 3rdFRIDAY of each month

12:00 –1:00 pm

High Quality MAT

2/05/21

Determining Levels of Care

Caitlin Kratz, MSW,LISW-CP,LAC,AADC

2/19/21

Non Pharmacological Treatment of Chronic Pain

Lauren Linder, PharmD