Long-acting Buprenorphine Treatment for Opioid Use Disorder

Michelle Lofwall, MD, DFAPA
Professor of Behavioral Science and Psychiatry
University of Kentucky College of Medicine
Center on Drug and Alcohol Research

Tuesday, February 11th, 2020
12:00 PM – 1:00 PM EST
Webinar Housekeeping

Minimize or maximize the webinar panel by selecting the orange arrow.

To be recognized, type your question in the “Question” box and select send.
Disclosures

I have relevant financial relationships with two ACCME-defined commercial interests:

1. I have been a consultant for Titan Pharmaceuticals regarding OUD and their new indications/formulations and study designs.

2. I have received stipends and reimbursements from Camurus for developing talks on research conducted with their OUD buprenorphine injectables.
Outline for Today’s Discussion

• Potential benefits of long-acting buprenorphine (bup) medications
  ▪ How can they help us move forwards to improve opioid use disorder (OUD) treatment access, retention and remission?

• Three different products

• Conclusions
Moving forwards: **Who** may benefit?

- Patients with difficult transitions – e.g., leaving a hospital, emergency room, jail.
  

**Emergency department-initiated buprenorphine/naloxone treatment for opioid dependence: a randomized clinical trial.**

D’Onofrio G1, O’Connor PG2, Pantalon MV1, Chawarsi MC3, Busch StH4, Owens PH1, Bernstein SL1, Fiellin DA5.

- 2-fold increase in attending the first outpatient appointment if started sublingual BUP in the ER (78% vs. 37%). But many providers hesitant to prescribe because of concerns about diversion and misuse of sublingual BUP—what if they could just give a shot?

- Pregnant women and newborns – might there be better outcomes from steady medication levels? Study underway.

- Patients at risk for non-adherence and misuse
  - Unstable living situations, transportation problems, addicted to injection

- Patient preference (e.g., no need for pharmacy visits, supervised dosing)
Moving forwards: Where to deliver long-acting treatments?

- John Dillinger: infamous bank robber from the 1930s. “Why do you rob banks?”…“Because that’s *where* the money is.”
- Where are our potential patients?
  - Criminal justice
  - Emergency rooms, hospitals and primary care
  - Homeless
  - Must bring treatment to patients
Overview of long-acting buprenorphine products

<table>
<thead>
<tr>
<th>Approval</th>
<th>6-month implants (Sixmo®/Probuphine®)</th>
<th>Monthly injection (Sublocade®)</th>
<th>Weekly and monthly injection (Buvidal®/Brixadi®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval</td>
<td>EMA &amp; USA</td>
<td>Australia &amp; USA</td>
<td>Australia, EMA, USA*</td>
</tr>
<tr>
<td>Indications</td>
<td>Clinically stable adults with OUD, already on SL bup 8mg/day or less and already receiving medical, psychological and social support</td>
<td>Adults with moderate-severe OUD, tolerating SL bup at 8-24 mg/day for at least 7 days. Counseling and psychological support should be part of treatment plan.</td>
<td>Treatment OUD (age 16yrs +) within framework of medical, psychological and social treatment</td>
</tr>
<tr>
<td>Mean bup concentration at steady state (ng/mL)</td>
<td>~0.82</td>
<td>100 mg injection: 3.21 300 mg injection: 6.54</td>
<td>Variable depending on dose but &gt;1</td>
</tr>
<tr>
<td>Minor surgical procedure required</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Medication administration site</td>
<td>Upper arm - subdermal</td>
<td>Abdomen –subcutaneous (SC)</td>
<td>Abdomen, arm, leg, buttock (SC)</td>
</tr>
<tr>
<td>Refrigeration required?</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Solid Matrix Subdermal Implant
FDA-approved May 2016

- EVA polymer
  Inert component of several approved products
- Buprenorphine

Blended & Extruded

26 mm long, 2.5 mm diameter, 80 mg buprenorphine/rod

- 4 rods (320mg buprenorphine) provide sustained release of buprenorphine for up to 6 months.
- Remove and replace after 6 months.
- Peak concentration 12 hours after placement.
- Serious adverse events: uncommon but possible including migration and nerve damage, potential for extraction and misuse.

Clinical stability criteria

- Period free from illicit opioid drug use
- Stability of living environment
- Participation in a structured activity/job
- Consistency in participation in recommended behavioral therapy/peer support program
- Consistency in compliance with clinic visit requirements
- Minimal to no desire or need to use illicit opioids
- Period without episodes of hospitalizations (addiction or mental health issues), emergency room visits, or crisis intervention
Effect of Buprenorphine Implants on Illicit Opioid Use Among Abstinent Adults With Opioid Dependence Treated With Sublingual Buprenorphine: A Randomized Clinical Trial.

Richard N. Rosenthal, MD.; Michelle R. Lofwall, MD; Sonnie Kim, PharmD; Michael Chen, PhD; Katherine L. Beebe, PhD.; Frank J. Vocci, PhD.; PRO-814 Study Group


<table>
<thead>
<tr>
<th>Responder rate</th>
<th>Implant</th>
<th>SL Bup/naloxone</th>
<th>P value</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Analysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• At least 4 of 6 months without illicit opioid use</td>
<td>81/84 (96.4%)</td>
<td>78/89 (87.6%)</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11.4</td>
</tr>
<tr>
<td><strong>Secondary Analysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• All 6 months without illicit opioid use</td>
<td>72/84 (85.7%)</td>
<td>64/89 (71.9%)</td>
<td>0.03&lt;sup&gt;b&lt;/sup&gt;</td>
<td>7.3</td>
</tr>
</tbody>
</table>

177 randomized; 166 completed (93.8% retention!!)

Consider SL supplementation if destabilize – 17.9% required SL, and it was low dose (2/0.5) and for a short period.

<sup>a</sup> Non-inferiority.  <sup>b</sup> Superiority
Relative use of SL buprenorphine/naloxone tablets

Data courtesy of Dr. Sonnie Kim, Braeburn Pharmaceuticals, an Apple Tree Company
Conclusions about implant

- Implants targeting a subpopulation and suggesting potential benefit over standard treatment
- Patients report liking not to dose themselves daily, not having to worry when traveling or if need to reschedule
- Limited uptake in USA – many barriers
- Questions remain – Different locations besides the arm? How to make it easier for patients and providers to access?
RBP-6000: Monthly subcutaneous buprenorphine
FDA-approved November 2017

- Comes in prefilled 19-gauge syringe.
- Refrigerate, keep at room temperature for at least 15 minutes prior to injection
- Dose: Months one and two = 300 mg, month 3 and thereafter = 100 mg (may increase if clinically indicated).
- Obtain baseline LFTS and monitor monthly, particularly with 300 mg dose.
- Most common side effects were: nausea, vomiting, headache, constipation, increased LFTs, tiredness, injection site itching and pain. Uncommon: need for surgical removal of injection.
- Also, limited uptake in USA although better than the implants.
Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial

Barbara R Haight, Susan M Learned, Celine M Laffont, Paul J Fudala, Yue Zhao, Amanda S Garofalo, Mark K Greenwald, Vijay R Nadipelli, Walter Ling, Christian Heidbreder, for the RB-US-13-0001 Study Investigators*

- Treatment seeking adults age 18-65 years with mod-severe OUD
- Two weeks open-label SL buprenorphine/naloxone film (n=665)
- If still eligible, randomized (n=504) 4:4:1 to:
  - BUP-XR 300 mg/300 mg (six injections of 300 mg every 28 days; n=201),
  - BUP-XR 300 mg/100 mg (two injections of 300 mg plus four injections of 100 mg; n=203),
  - Placebo injections every 28 days (n=100)
- Individual counseling throughout trial
- No prn SL buprenorphine/naloxone available
- Primary outcome: % abstinence from opioids by urine tests from weeks 5-24 confirmed by self-report
### Randomized sample characteristics

<table>
<thead>
<tr>
<th></th>
<th>300mg/300mg</th>
<th>300mg/100mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, yrs (SD)</td>
<td>39.3 (11.0)</td>
<td>40.4 (11.2)</td>
<td>39.2 (11.0)</td>
</tr>
<tr>
<td>Male, no. (%)</td>
<td>132 (67)</td>
<td>128 (66)</td>
<td>64 (65)</td>
</tr>
<tr>
<td>White, no. (%)</td>
<td>140 (71)</td>
<td>132 (68)</td>
<td>77 (78)</td>
</tr>
<tr>
<td>Mean BMI (SD)</td>
<td>26.4 (4.4)</td>
<td>25.3 (4.2)</td>
<td>25.3 (4.3)</td>
</tr>
<tr>
<td>Injection opioid use, no. (%)</td>
<td>79 (41)</td>
<td>84 (43)</td>
<td>50 (51)</td>
</tr>
<tr>
<td>Hep C +, no. (%)</td>
<td>24 (12)</td>
<td>31 (16)</td>
<td>10 (10)</td>
</tr>
</tbody>
</table>
Retention after randomization

Number at risk

<table>
<thead>
<tr>
<th>Group</th>
<th>Days on Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUP-XR 300 mg/300 mg + IDC</td>
<td>196 193 170 152 144 134 95</td>
</tr>
<tr>
<td>BUP-XR 300 mg/100 mg + IDC</td>
<td>194 185 167 153 148 141 80</td>
</tr>
<tr>
<td>Placebo + IDC</td>
<td>99 69 57 48 44 39 23</td>
</tr>
</tbody>
</table>
Opioid withdrawal
Opioid craving

[Graph showing mean opioid craving VAS score (95% CI) over time since randomisation (weeks) with different lines representing different treatment groups: BUP-XR 300 mg/300 mg + IDC, BUP-XR 300 mg/100 mg + IDC, Placebo + IDC.]
Opioid use outcomes

<table>
<thead>
<tr>
<th></th>
<th>300mg/300mg  n=196</th>
<th>300mg/100mg  n=194</th>
<th>Placebo  n=99</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong>:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean % abstinent</td>
<td>41.3% (39.7%)</td>
<td>42.7% (38.5%)</td>
<td>5.0% (17.0%)</td>
</tr>
<tr>
<td><strong>Key secondary</strong>:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># ≥80% abstinent</td>
<td>57 (29%)</td>
<td>55 (28%)</td>
<td>2 (2%)</td>
</tr>
</tbody>
</table>

*Figure 5: Proportion of participants abstinent by week*

Missing measure of either urine drug screen or timeline followback interview at a week was imputed as positive opioid use. Week 0 represents the opioid usage assessment at screening, and week 1 represents the opioid usage assessment at week 1, day 1 visit (baseline). IDC=individual drug counselling.
### Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>BUP-XR 300/300 mg plus individual drug counselling (n=201)</th>
<th>BUP-XR 300/100 mg plus individual drug counselling (n=203)</th>
<th>Placebo plus individual drug counselling (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any treatment-emergent adverse event</td>
<td>134 (67%)</td>
<td>155 (76%)</td>
<td>56 (56%)</td>
</tr>
<tr>
<td>Any serious treatment-emergent adverse event</td>
<td>7 (3%)</td>
<td>4 (2%)</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>Any severe treatment-emergent adverse event</td>
<td>13 (6%)</td>
<td>15 (7%)</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Any treatment-emergent adverse event leading to discontinuation</td>
<td>10 (5%)</td>
<td>7 (3%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Any treatment-emergent adverse event leading to death</td>
<td>1 (&lt;1%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

- One non-fatal opioid overdose in the placebo group
- Most participants (96%) reported local burning or stinging at the injection site, peaking about 1 minute after injection
- No injection required removal
- Some BUP XR LFT elevation but none met criteria for Hy’s Law. FDA label recommends monitoring LFT, particularly with the 300 mg dose.
FIGURE 1. Percentage of subjects who were satisfied or dissatisfied with treatment at week 25\textsuperscript{a}. BUP-XR, buprenorphine extended-release monthly injection, for subcutaneous use [CII]; IDC, individual drug counselling; MSQ, Medication Satisfaction Questionnaire. \textsuperscript{a}The MSQ is a 7-point scale with the following ratings: 1, extremely dissatisfied, 2, very dissatisfied, 3, somewhat dissatisfied, 4, neither satisfied nor dissatisfied, 5, somewhat satisfied, 6, very satisfied, and 7, extremely satisfied. MSQ scores were categorized as satisfied (5–7), neutral (4), or dissatisfied (1–3).
Subcutaneous weekly and monthly CAM2038

- Approved 2018 in Europe & Australia, tentative approval USA 2018 – exclusivity issue
- Weekly & monthly formulations with multiple doses
- Store at room temperature
- Pre-filled syringes with safety device
- Small volume (<1 mL), thin needle
- Several injection site locations

BUP-Sublingual

<table>
<thead>
<tr>
<th>dosage</th>
<th>CAM2038 weekly</th>
<th>CAM2038 monthly</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 mg</td>
<td>8 mg (0.16 mL)</td>
<td>--</td>
</tr>
<tr>
<td>8-10 mg</td>
<td>16 mg (0.32 mL)</td>
<td>64 mg (0.18 mL)</td>
</tr>
<tr>
<td>12-16 mg</td>
<td>24 mg (0.48 mL)</td>
<td>96 mg (0.27 mL)</td>
</tr>
<tr>
<td>18-24 mg</td>
<td>32 mg (0.64 mL)</td>
<td>128 mg (0.36 mL)</td>
</tr>
</tbody>
</table>

BUP-SL dose and approximate equivalent weekly and monthly BUP-XR injections

NOTE: BUP-SL doses are in Subutex® equivalents

FluidCrystal® nano-technology

Phase 2 Study: Purpose, Design & Eligibility

- Evaluate withdrawal suppression and blockade efficacy of weekly CAM2038

- 3-week inpatient, double-blind randomized within subject study

- Non-treatment seeking adults with moderate-severe opioid use disorder (OUD), otherwise healthy
Methods

- Initial stabilization: Morphine 30 mg orally 4 times daily
- Qualification phase: Hydromorphone (HM 0, 6, 18 mg, IM; random order) – to ensure sensitive & like HM effects
- Randomized 1:1 to either:
  - CAM2038 24 mg weekly injections (~16 mg SL buprenorphine)
  - CAM2038 32 mg weekly injections (~24 mg SL buprenorphine)
- Four sets of HM challenge sessions

Walsh, Comer, Lofwall et al. Effect of Buprenorphine Weekly Depot (CAM2038) & Hydromorphone Blockade in Individuals with Opioid Use Disorder. *JAMA Psychiatry.* 2017 Sep 1;74(9):894-902.
“At this moment, my liking for drug is”
Mental State (Drowsy to Alert)

![Graph showing peak scores over time with injection points at days 0, 6, and 18. The graph compares two groups: CAM 2038 24 mg and CAM 2038 32 mg. The x-axis represents days, and the y-axis represents peak score (mm). The graph shows a decrease in peak score over time for both groups with distinct markers for each injection point.]
Clinical Opiate Withdrawal Scale

The diagram shows the total score over the treatment duration for two groups: CAM2038 24 mg and CAM2038 32 mg. The score remains relatively stable throughout the treatment duration.
Results

• Blockade of liking, high, good effects

• Diminished craving and rapid withdrawal suppression (without need for a sublingual buprenorphine lead-in)

• No SAEs – constipation most common side effect
Phase 3 randomized, double-blind, double-dummy, active control study

Counseling, UDT, self-report drug use, craving, and withdrawal assessed at each visit

Lofwall, Walsh, Nunes et al. Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine with Naloxone for Treatment of Opioid Use Disorder: A Randomized Clinical Trial. *JAMA Internal Medicine* 2018
Primary Outcomes

• European Medicines Agency: Proportion of urine toxicology results negative for illicit opioids

• US Food and Drug Administration: Responder rate whereby a responder required to have no illicit opioid-positive urines (supported by self-report) in:
  - Phase 1: at Week 12 and for at least 2 of the 3 weeks between Weeks 9–11, and in
  - Phase 2: during Month 6 (Weeks 21–24) and for at least 5 of the 6 assessments during Weeks 13–24.

<table>
<thead>
<tr>
<th>Week</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHASE 1 (WEEKS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>R</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Week</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHASE 2 (MONTHS)</td>
<td>R</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• Note: Highly sensitive urine testing: 5 ng/mL was the lower limit of detection for codeine, morphine, hydrocodone, oxycodone; also tested for methadone and its metabolite, oxymorphone, fentanyl and norfentanyl
Baseline sample characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SL BPN/NX (n=215)</th>
<th>CAM2038 (n=213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>38.0 (10.9)</td>
<td>38.7 (11.2)</td>
</tr>
<tr>
<td>Male, No. (%)</td>
<td>142 (66.0)</td>
<td>121 (56.8)</td>
</tr>
<tr>
<td>White, No. (%)</td>
<td>164 (76.3)</td>
<td>159 (74.6)</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>26.2 (5.6)</td>
<td>25.6 (5.0)</td>
</tr>
<tr>
<td>Employed, No. (%)</td>
<td>72 (33.5)</td>
<td>76 (35.7)</td>
</tr>
<tr>
<td>History of any arrest, No. (%)</td>
<td>144 (67.0)</td>
<td>130 (61.0)</td>
</tr>
<tr>
<td>Primary opioid of use, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>151 (70.2)</td>
<td>152 (71.4)</td>
</tr>
<tr>
<td>Prescription opioids</td>
<td>64 (29.8)</td>
<td>61 (28.6)</td>
</tr>
<tr>
<td>Injection use history, No. (%)</td>
<td>110 (51.2)</td>
<td>114 (53.5)</td>
</tr>
<tr>
<td>Hepatitis C antibody pos., No (%)</td>
<td>81 (37.7)</td>
<td>81 (38.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SL BPN/NX (n=215)</th>
<th>CAM2038 (n=213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl + screening, No. (%)</td>
<td>42 (22.8)</td>
<td>62 (29.1)</td>
</tr>
<tr>
<td>Non-opioid drug use screening, No. (%)</td>
<td>149 (69.3)</td>
<td>155 (72.8)</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>32 (14.9)</td>
<td>38 (18.0)</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>35 (16.3)</td>
<td>30 (14.2)</td>
</tr>
<tr>
<td>Cocaine</td>
<td>53 (24.7)</td>
<td>53 (25.1)</td>
</tr>
<tr>
<td>Marijuana</td>
<td>64 (29.8)</td>
<td>57 (27.0)</td>
</tr>
</tbody>
</table>

Baseline opioid craving and withdrawal scores, mean (SD)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SL BPN/NX (n=215)</th>
<th>CAM2038 (n=213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Craving: need to use VAS (0–100)</td>
<td>76 (24.9)</td>
<td>77 (25.4)</td>
</tr>
<tr>
<td>Craving: desire to use VAS (0–100)</td>
<td>77 (25.4)</td>
<td>77 (26.2)</td>
</tr>
<tr>
<td>COWS score (0–48)</td>
<td>12 (6.0)</td>
<td>12 (5.4)</td>
</tr>
<tr>
<td>SOWS score (0–64)</td>
<td>31 (16.1)</td>
<td>32 (15.4)</td>
</tr>
</tbody>
</table>

No significance difference between groups
Medication dose

![Graph showing SC BPN dose over treatment weeks.](image)

- **SC CAM 2038**
- **SL BPN/NX**

**Axes:**
- **Y-axis:** SC BPN dose (mg)
- **X-axis:** Treatment Week

**Legend:**
- Weekly Injections
- Monthly Injections
# Primary Endpoints
(Intent to treat analyses for non-inferiority)

<table>
<thead>
<tr>
<th></th>
<th>SL BPN/NX</th>
<th>SC CAM2038</th>
<th>P-value non-inferiority</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA:</strong> Responder rate</td>
<td>n=31, 14.4%</td>
<td>n=37, 17.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Difference %, (95% CI)</td>
<td>3.0% (-4.0%, 9.9%)</td>
<td>Non-inferiority margin: 10%</td>
<td></td>
</tr>
<tr>
<td><strong>EMA:</strong> Mean % opioid negative urine</td>
<td>28.4%</td>
<td>35.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Difference %, (95% CI)</td>
<td>6.7% (-0.1%, 13.6%)</td>
<td>Non-inferiority margin: 11%</td>
<td></td>
</tr>
</tbody>
</table>
Urine tests with self-report

Missing samples imputed as positive. All negative urines supported by self-report. BL, baseline. * indicates significant difference at that time point.
“Since your last scheduled visit, indicate your worst or strongest need to use opioids between 0 (No Need to Use) and 100 (Maximum Need to Use) on this scale.”

No significant difference between treatments
Clinical opiate withdrawal scale

No significant difference between treatments
Distribution of percent opioid-negative weeks (with self-reports) in group with injection use at baseline (Weeks 4-24)

- SC CAM 2038 (n=114)
- SL BPN/NX (n=110)

P<0.001
### Adverse events

<table>
<thead>
<tr>
<th>Adverse event (AE) characteristic</th>
<th>SL-BPN/NX (n = 215)</th>
<th>CAM2038 (n = 213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-fatal serious</td>
<td>13 (6.0%)</td>
<td>5 (2.3%)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Hospitalisations</td>
<td>12 (5.6%)</td>
<td>3 (1.4%)</td>
</tr>
<tr>
<td>Drug overdoses</td>
<td>5 (2.3%)</td>
<td>0</td>
</tr>
<tr>
<td>Led to discontinuation of treatment</td>
<td>3 (1.4%)</td>
<td>7 (3.3%)</td>
</tr>
</tbody>
</table>

**Treatment emergent AE in >5% of participants**

<table>
<thead>
<tr>
<th>Condition</th>
<th>SL-BPN/NX (n = 215)</th>
<th>CAM2038 (n = 213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection site pain</td>
<td>17 (7.9%)</td>
<td>19 (8.9%)</td>
</tr>
<tr>
<td>Headache</td>
<td>17 (7.9%)</td>
<td>16 (7.5%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>16 (7.4%)</td>
<td>16 (7.5%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>17 (7.9%)</td>
<td>15 (7.0%)</td>
</tr>
<tr>
<td>Injection-site pruritus</td>
<td>13 (6.0%)</td>
<td>13 (6.1%)</td>
</tr>
<tr>
<td>Injection-site erythema</td>
<td>12 (5.6%)</td>
<td>12 (5.6%)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>10 (4.7%)</td>
<td>11 (5.2%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>6 (2.8%)</td>
<td>12 (5.6%)</td>
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</tbody>
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Overall, CAM2038 safety profile comparable to daily SL with addition of injection site reactions, which all were mild (74%) or moderate (26%) severity.
Open-label study: Patient ratings of important features of CAM2038 (N=133)

Among patients switching from SL BUP to SC BUP in an open-label study, majority (83%) rate SC BUP as "somewhat better" or "much better" compared to SL.

Clinical Study Report (CSR) HS 14 499  Figure courtesy of Sonnie Kim, Pharm D Braeburn Pharmaceuticals. Frost, Bailey et al. Long-term safety of a weekly and monthly subcutaneous buprenorphine depot (CAM2038) in the treatment of adult outpatients with opioid use disorder. Addiction 2019.
Conclusions

• Long-acting medications for OUD hold much promise for improving treatment entry, retention and patient outcomes

• Look forward to many ongoing studies and learning about real world clinical implementation and effectiveness
References


• TIP 63 Medications for Opioid Use Disorder [available for free download @ https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder]

• Walsh, Comer, Lofwall et al. Effect of Buprenorphine Weekly Depot (CAM2038) & Hydromorphone Blockade in Individuals with Opioid Use Disorder. JAMA Psychiatry.2017 Sep 1;74(9):894-902.
PCSS Mentoring Program

- PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid use disorder.

- PCSS Mentors are a national network of providers with expertise in addictions, pain, evidence-based treatment including medications for addiction treatment.
  - 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.
  - No cost.

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<td>American Society for Pain Management Nursing</td>
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<tr>
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<td>Association for Multidisciplinary Education and Research in Substance use and Addiction</td>
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<tr>
<td>American Academy of Pediatrics</td>
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