First Dose Treatment Effects With Injectable Weekly and Monthly Buprenorphine and the Relationship Between Buprenorphine Plasma Concentrations and Withdrawal Suppression in Participants With Opioid Use Disorder

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BACKGROUND

- Early studies examining the relationship between buprenorphine (BPN) plasma concentrations and opioid withdrawal in patients with opioid use disorder (OUD) reported an association between higher BPN plasma levels and withdrawal suppression and suggested that opioid withdrawal was controlled at 1 to 2 ng/mL.[1–3]
- More recent data, however, have shown that opioid withdrawal is effectively suppressed in most patients with OUD at relatively lower BPN plasma concentrations.[4,5]
- Brixadi® (CAM2038) is a weekly and monthly injectable BPN medication approved for the treatment of moderate-to-severe OUD, which has demonstrated withdrawal suppression and illicit opioid use reduction.[6,7]

METHODS

- An open-label, single-dose, pharmacokinetic (PK) study evaluated participants with moderate-to-severe OUD randomized to either CAM2038 32 mg weekly or 128 mg monthly.
- During the 2-week period preceding CAM2038 administration (Day -13 to Day 1), participants were assessed for self-reported illicit drug use using timeline follow back (TLFB).
- Prior to CAM2038 administration on Day 1, Clinical Opiate Withdrawal Scale (COWS) scores (mild = 5 to 12; moderate = 13 to 24; moderately severe = 25 to 36; severe = >36) were collected.
- Following CAM2038 administration, participants remained inpatient for 5 days (Day 2 to Day 6) and returned for outpatient visits at Day 8 (last visit for CAM2038 weekly group), Day 15, Day 22, and Day 29.
- PK samples and COWS scores were collected each inpatient day and at subsequent outpatient visits; illicit drug use was assessed at each outpatient visit.
- A post hoc analysis (N=110) evaluated the effect of single-dose CAM2038 32 mg weekly and 128 mg monthly on opioid withdrawal and self-reported illicit drug use and characterized the association between BPN plasma concentrations and withdrawal suppression (defined as COWS <5).

RESULTS

- The mean baseline COWS score on Day 1 was approximately 13 and no participants recorded a score <5; by Day 2, 52.5% (CAM2038 weekly) and 32.3% (CAM2038 monthly) of participants had COWS scores <5, which increased to 68.4% and 60.7% by Day 3 and to 91.2% and 94.5% by the end of the dosing interval.
- No meaningful association was observed between BPN plasma concentrations and opioid withdrawal suppression across study time points (**Figure 2**).

Figure 1. Mean COWS Scores Over Time by Treatment Group

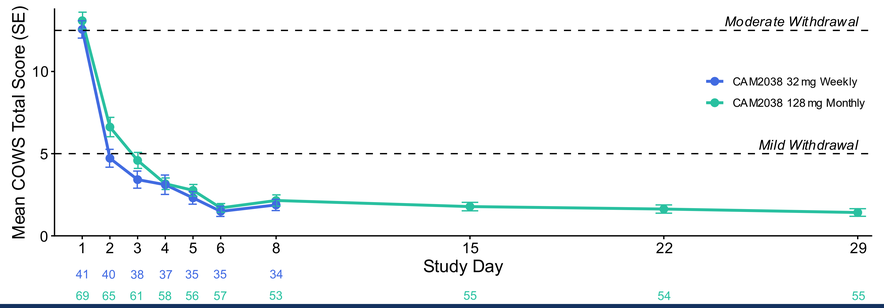
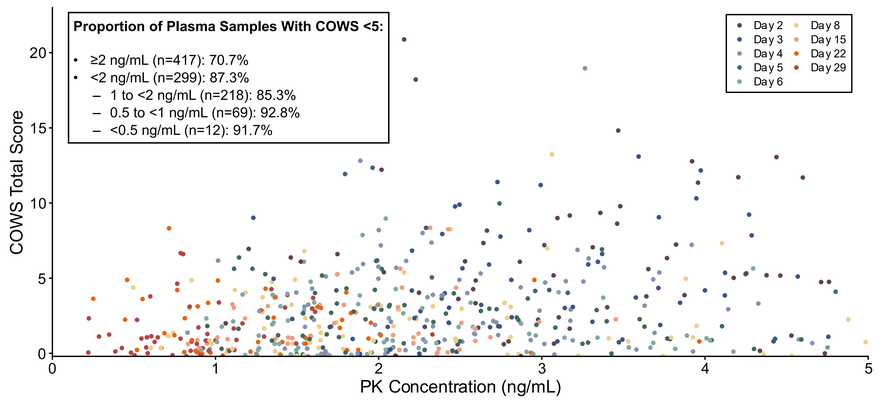


Figure 2. COWS Scores vs BPN Plasma Concentrations by Study Day (0-5 ng/mL)*



*BPN plasma samples >5 ng/mL are not shown.

- Self-reported illicit opioid use among all participants declined from 93.5% at baseline to 14.3% (CAM2038 weekly) and 17.6% (CAM2038 monthly) by the end of the dosing interval, respectively (**Table 1**).
- Reductions in self-reported use of other illicit substances were also observed following administration of CAM2038 32 mg weekly and 128 mg monthly (**Table 1**).

Table 1. Self-Reported Illicit Drug Use Over Time by Treatment Group*

1A. CAM2038 32 mg Weekly

Substance	Baseline (n=40)	Week 1 (n=28)
Opioids	95.0%	14.3%
Cannabis	40.0%	35.7%
Benzodiazepines	2.5%	0.0%
Amphetamines	40.0%	7.1%
Cocaine	5.0%	0.0%
Crack	5.0%	0.0%

1B. CAM2038 128 mg Monthly

Baseline (n=68)	Week 1 (n=56)	Week 2 (n=52)	Week 3 (n=52)	Week 4 (n=51)
92.6%	14.3%	23.1%	17.3%	17.6%
47.1%	28.6%	28.8%	32.7%	29.4%
11.8%	5.4%	3.8%	1.9%	2.0%
39.7%	25.0%	21.2%	21.2%	13.7%
17.6%	0.0%	7.7%	1.9%	3.9%
11.8%	3.6%	5.8%	3.8%	2.0%

*Participants were inpatient from Day 1 to Day 6; self-reported illicit drug use was assessed by TLFB prior to Day 1 administration (baseline) and at outpatient visits on Day 8 (Week 1; lighter blue = inpatient/outpatient), Day 15 (Week 2), Day 22 (Week 3), and Day 29 (Week 4). TLFB = timeline follow back.

LIMITATIONS

- This analysis was post hoc and exploratory and was not prospectively designed to evaluate the relationship between BPN plasma concentrations and opioid withdrawal.
- Results were based on participants treated with single-dose weekly and monthly CAM2038 and further research may be valuable to confirm these findings in a broader clinical context.

CONCLUSIONS

- Rapid and sustained opioid withdrawal suppression was observed in participants with moderate-to-severe OUD treated with weekly and monthly CAM2038.
  - COWS scores <5 were consistently recorded in participants at the end of the weekly and monthly dosing interval, including in those with the lowest observed BPN plasma concentrations.
- Self-reported illicit use of opioids and other drugs declined across weekly and monthly dosing intervals.
- These findings reinforce known treatment effects of weekly and monthly CAM2038 and indicate that very low BPN plasma concentrations (<0.5 ng/mL) effectively suppress withdrawal and illicit opioid use

REFERENCES

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DISCLOSURES

Michael P. Frost has received consulting/speaking honoraria from Braeburn Inc, consultant fees from Molteni Farmaceutici and Accord Healthcare, and is a shareholder of Pinova Therapeutics. Edward V. Nunes is an investigator on NIH-funded studies that have received in-kind donations of medications or digital therapeutics from Braeburn Inc, Camurus AB, CHESS Health, Indivior, and Pear Therapeutics. Michelle R. Lofwall has received consultant fees from Berkshire Biomedical, Braeburn Inc, and Sophrosyne Pharmaceuticals and honorarium for a research talk from Camurus in the last 3 years. Sharon L. Walsh has received consultant fees for advising on the development and use of products for the treatment of OUD from Cerevel Therapeutics, Braeburn Inc, Kinoxis Therapeutics, Reacx Pharmaceuticals, Titan Pharmaceuticals, and Opiant Pharmaceuticals, and has participated in advisory board meetings with Braeburn Inc in the last 3 years. Genie L. Bailey has received consulting/speaking honoraria from Braeburn Inc. Brian J. Dawson has received consulting/speaking honoraria from Braeburn Inc. Natalie R. Budilovsky-Kelley, Adam Friedman, Carrie Kaempfer, and Joshua M. Cohen are current employees of Braeburn Inc.

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