Efficacy and Safety Comparison of Weekly/monthly Extended-release Injectable Buprenorphine (CAM2038) vs Daily Sublingual Buprenorphine/naloxone (BPN/NX) for Treatment of Patients with OUD Who Opioids or Use Heroin

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BACKGROUND

- Heroin and injection drug use are associated with treatment attrition and opioid misuse during treatment for opioid use disorder (OUD)[1]
- Daily sublingual buprenorphine/ naloxone (SL BPN/NX) is known to be effective for the treatment of OUD, however treatment response is typically lower in people that use heroin or people who inject opioids (PWIO)[1]
- People who inject drugs (PWID) are susceptible to serious health hazards including blood-borne diseases and bacterial skin, soft tissue, and blood infections, with up to 32% of PWID affected by cellulitis and skin or soft tissue abscesses at a given time[2,3]
- In the United States, heroin is increasingly available in larger quantities and increasing purity, used by a greater number of people, and is causing an increasing number of overdose deaths, with an estimated 15,958 deaths from heroin-related overdoses in 2017[4,5]
- CAM2038, weekly or monthly subcutaneous (SC) BPN, is a ready-to-use, extended-release injection, with multiple dosing options for the treatment of OUD[6]

METHODS

- Phase 3, outpatient, double-blind, double-dummy, active-controlled, parallel group, multi-center study was conducted to evaluate the non-inferiority of CAM2038 compared with an existing standard of care, daily SL BPN/NX, in BPN initiation and maintenance treatment[6]
- Participants were randomized to CAM2038 or SL BPN/NX on day 1 of treatment initiation. Phase 1 (first 12 weeks) required weekly visits with both daily dosing and weekly injections. Participants transitioned to monthly visits during Phase 2 (second 12 weeks) with both daily dosing and monthly injections. (daily dosing = either SL BPN/NX or matching placebo; weekly or monthly injections = either CAM2038 or matching placebo injections)[6]
- A post-hoc analysis was conducted (intent-to-treat [ITT] population) to assess efficacy of CAM2038 compared with SL BPN/NX in treating participants for whom heroin was the primary opioid of use at baseline and participants who used injection as route of illicit opioid use (PWIO)[6]

RESULTS

- Of the 428 participants randomized, 224 (52.33%) identified injection as the preferred route of illicit opioid use (PWIO) and 303 (70.8%) identified heroin as the primary opioid of use at baseline **(Table 1)**
- Demographics and clinical characteristics were similar between treatment groups in PWIO and participants identifying heroin as the primary opioid of use at baseline **(Table 1)**

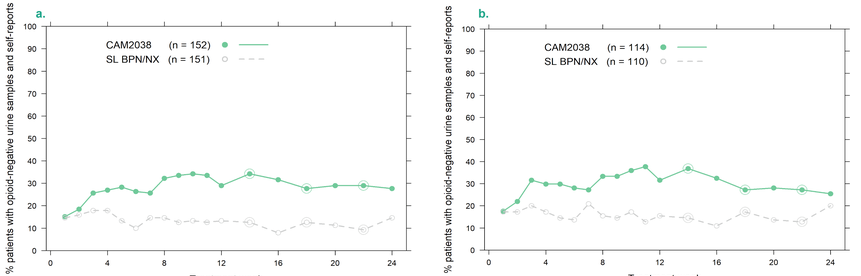
Table 1. Demographics and Baseline Clinical Characteristics by Treatment and Fentanyl Use at Baseline

CATEGORY	HEROIN			PWIO		
	CAM2038 N = 152	SL BPN/NX N = 151	TOTAL N=303	CAM2038 N = 114	SL BPN/NX N = 110	TOTAL N=224
Age, mean (SD), y	38.9 (11.2)	38.9 (11.4)	38.9 (11.3)	37.32 (11.65)	37.15 (11.54)	37.24 (11.57)
Male, No. (%)	86 (56.6)	105 (69.5)	191 (63.0)	62 (54.4)	73 (66.4)	135 (60.3)
White, No. (%)	101 (66.4)	105 (69.5)	206 (68.0)	90 (78.9)	91 (82.7)	181 (80.8)
BMI, mean (SD), kg/m²	25.2 (4.9)	25.5 (4.9)	25.3 (4.9)	25.01 (4.89)	25.41 (4.97)	25.21 (4.92)
Duration since OUD diagnosis, mean (SD), y	4 (8.74)	3.19 (4.67)	3.72 (7.44)	3.06 (5.29)	2.76 (3.54)	2.95 (4.66)
Injection route of illicit opioid use, No. (%)	97 (63.8)	95 (62.9)	192 (63.4)	114 (100)	110 (100)	224 (100)
Heroin primary opioid of use, No. (%)	152 (100)	151 (100)	303 (100)	97 (85.1)	95 (86.4)	192 (85.7)
Utox Fentanyl positive at screening, No. (%)	54 (35.5)	39 (25.8)	93 (30.7)	36 (31.6)	24 (21.8)	60 (26.8)
Nonopioid drug use at screening, No (%):	135 (88.8)	142 (94)	277 (91.4)	95 (83.3)	101 (91.8)	196 (87.5)
Methamphetamine	27 (17.8)	25 (16.6)	52 (17.2)	21 (18.4)	23 (20.9)	44 (19.6)
Benzodiazepine	18 (11.8)	23 (15.2)	41 (13.5)	12 (10.5)	13 (11.8)	25 (11.2)
Marijuana	39 (25.7)	47 (31.1)	86 (28.4)	28 (24.6)	32 (29.1)	60 (26.8)
Cocaine	51 (33.6)	47 (31.1)	98 (32.3)	34 (29.8)	33 (30.0)	67 (29.9)
Hep. C antibody positive at screening, No. (%)	71 (46.7)	70 (46.4)	141 (46.5)	72 (63.2)	73 (66.4)	145 (64.7)
COWS, mean (SD)	11.7 (4.79)	11.9 (5.95)	11.8 (5.39)	11.81 (5.27)	12.06 (6.58)	11.93 (5.94)
SOWS, mean (SD)	32.0 (14.9)	31.4 (167)	31.7 (15.8)	30.54 (14.53)	31.23 (17.28)	30.88 (15.91)
Desire to use VAS (SD)	76.2 (26.7)	77.1 (24.6)	76.6 (25.8)	76.78 (25.48)	77.71 (25.76)	77.24 (25.57)
Need to use VAS (SD)	75.4 (26.3)	76.0 (25.7)	75.7 (26.0)	74.38 (26.92)	76.43 (25.90)	75.39 (26.38)

Data presented as n (%) unless otherwise noted. Body mass index (BMI); Clinical opioid withdrawal scale (COWS); Graduate equivalency exam (GED); Standard deviation (SD); Sublingual buprenorphine/naloxone (SL BPN/NX); Subjective opioid withdrawal scale (SOWS); Visual analog scale (VAS)

- For participants identifying heroin as the primary opioid of use the retention rate was 56% for CAM2038 and 54% for SL BPN/NX; for PWIO the retention rate was 55% for CAM2038 and 49% for SL BPN/NX

Figure 1. Percent of negative opioid assessments (urinalysis with self-report) over time for a. heroin users (n=303) and b. PWIO (n=224)



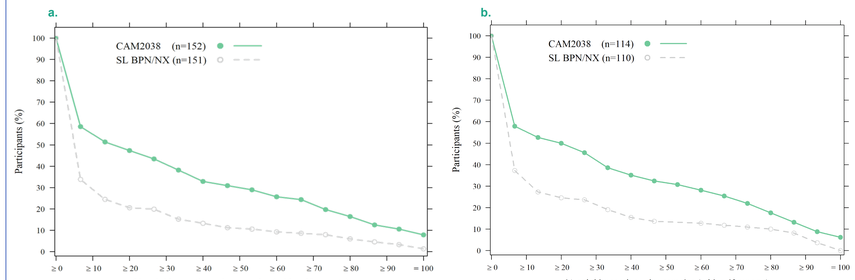
Open circles denote random samples. Random samples are the first, second, and third random sample, respectively, and these could occur in another period than shown

Percent negative opioid assessments (urinalysis and self-report; weeks 1-24)

Group	Treatment	Mean (%)	95% CI	p-value (ANOVA; non-inferiority)
Heroin users	CAM2038 (N=152)	28.2	7.8, 22.1	<0.001
	SL BPN/NX (N=151)	13.2		
PWIO	CAM2038 (N=114)	29.7	4.7, 23	<0.003
	SL BPN/NX (N=110)	15.9		

Sublingual buprenorphine/naloxone (SL BPN/NX); People who inject opioids (PWIO)

Figure 2. Cumulative Distribution Function (CDF) of percent of negative opioid assessments (urinalysis and self-report; weeks 4 to 24; ITT population) for a. heroin users (n=303) and b. PWIO (n=224)



p <0.001 (Wilcoxon; superiority)

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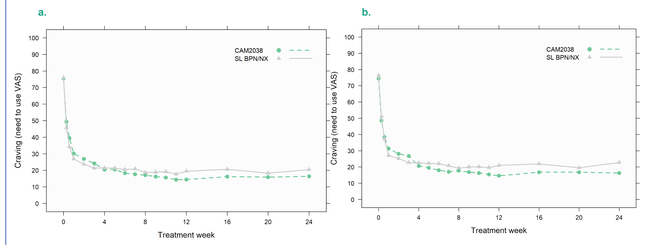
Group	Treatment	Median (%)	LS Mean (%)
Heroin users	CAM2038 (N=152)	13.3	29.9
	SL BPN/NX (N=151)	0	12.7
PWIO	CAM2038 (N=114)	16.7	30.9
	SL BPN/NX (N=110)	0	15.4

Sublingual buprenorphine/naloxone (SL BPN/NX); People who inject opioids (PWIO)

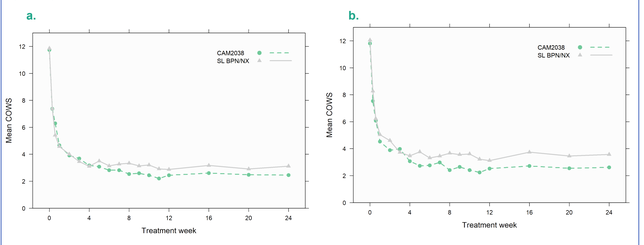
Figure 3. Mean craving assessed by Need to Use Visual Analog Scale (VAS)* for a. heroin users (n=303) and b. PWIO (n=224)



*Need to Use (opioid cravings) were assessed using unipolar 100 mm VAS (“Since your last scheduled assessment visit, indicate your worst or strongest need to use opioids, where 0 = No need to use and 100 mm = Strongest possible need)

Sublingual buprenorphine/naloxone (SL BPN/NX)

Figure 4. Mean Clinical Opioid Withdrawal Scale (COWS) score for a. heroin users (n=303) and b. PWIO (n=224)



Sublingual buprenorphine/naloxone (SL BPN/NX); People who inject opioids (PWIO)

Table 2. Summary of Treatment-Emergent Adverse Events (AEs)

System Organ Class/Preferred Term	HEROIN			PWIO		
	CAM2038 N = 152 n (%)	SL BPN/NX N = 151 n (%)	Total N=303 n (%)	CAM2038 N=114 n (%)	SL BPN/NX N=110 n (%)	Total N=224 n (%)
Infections and infestations	0	8 (5.3)	8 (2.6)	0	8 (7.3)	8 (3.6)
Abscess limb	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Acute hepatitis C	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Cellulitis	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Localized infection	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Osteomyelitis	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Pneumonia	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Sepsis	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Subcutaneous abscess	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Injury, poisoning and procedural complications	1 (0.6)	4 (2.6)	5 (1.6)	0	4 (3.6)	5 (2.2)
Accidental overdose	0	3 (2)	3 (1)	0	3 (2.7)	3 (1.3)
Intentional overdose	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Road traffic accident	1 (0.6)	0	1 (0.3)	0	0	0
Psychiatric disorders	0	3 (2)	2 (0.7)	0	3 (2.7)	2 (0.9)
Bipolar disorder	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Substance-induced mood disorder	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Suicidal ideation	0	1 (0.7)	2 (0.7)	0	1 (0.9)	2 (0.9)
Congenital, familial and genetic	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Haemophilia	0	1 (0.7)	1 (0.3)	0	1 (0.9)	1 (0.4)
Gastrointestinal disorders	0	0	0	1 (0.9)	0	1 (0.4)
Vomiting	0	0	0	1 (0.9)	0	1 (0.4)
Pregnancy, puerperium and perinatal conditions	1 (0.6)	0	1 (0.3)	1 (0.9)	0	1 (0.4)
Abortion spontaneous	1 (0.6)	0	1 (0.3)	1 (0.9)	0	1 (0.4)
General disorders and administration site conditions	1 (0.6)	0	1 (0.3)	0	0	0
Non-cardiac chest pain	1 (0.6)	0	1 (0.3)	0	0	0

- With the exception of injection site adverse events, the safety profile observed with CAM2038 was consistent with the known safety profile of SL BPN with no unexpected adverse events observed

CONCLUSIONS

- Treatment with CAM2038 increased the likelihood of no illicit opioid-use vs. BPN/NX in participants with poor prognostic factors, such as heroin use and PWIO
- CAM2038 demonstrated sustained opioid withdrawal and craving suppression from treatment initiation through maintenance for both heroin and injection users
- Safety profile comparable to that of SL BPN/NX with the exception of injection site reactions
- Weekly and monthly dosing options allow treatment providers the ability to individualize dosing based on evolving patient needs as done in current clinical practice

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CURRENT DISCLOSURES

EN serves or have served as an investigator on NIH funded studies that received in kind donations of medications or digital therapeutics from Alkermes, Braeburn, Camurus, Indivior, Pear Therapeutics, and CHESS Health, and have served as consultant without compensation for Alkermes, Camurus, Indivior, and Pear Therapeutics. ML received consulting fees from Titan and Journey Collab. SW served on an advisory board for Astra Zeneca, Opiant, and Titan and is a consultant for Cerevel and Pocket Naloxone. MF received consulting fees from Accord Healthcare, Molteni Farmaceutici and Knight Therapeutics and is a shareholder in Pocket Naloxone Corp. FT is an employee and shareholder of Camurus AB. NBK is an employee of Braeburn.

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