Poster 132

An efficacy and safety comparison of CAM2038 vs SL BPN/NX for the treatment of patients with OUD who inject opioids

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ABSTRACT

Aims: To report subgroup analyses for people who inject opioids (PWIO; n = 224) from a phase 3 trial comparing the extended-release depot injectable buprenorphine (CAM2038) to sublingual buprenorphine/naloxone (SL BPN/NX) among treatment-seeking adults with moderate-to-severe Opioid Use Disorder (OUD) (n = 428).

Methods: This 24-week, randomized, double-blind, double-dummy, active-controlled, parallel group, multi-center study, was designed to evaluate the non-inferiority of CAM2038 compared to an existing standard of care, SL BPN/NX, in initiation and maintenance treatment with buprenorphine. The prespecified primary endpoint was responder rate, with responder status defined as having no evidence of illicit opioid use for at least 8 of 10 prespecified points during weeks 9 to 24; with 2 of these at week 12 and during month 6 (weeks 21-24). A post-hoc subgroup analysis was conducted (ITT population) to assess efficacy of CAM2038 compared to SL BPN/NX in PWIO.

Results: Primary analysis demonstrated that CAM2038 (17.4%) was non-inferior to SL BPN/NX (14.4%) on the primary endpoint of responder rate. The percentage of responders for PWIO was higher in the CAM2038 group (15.8%) compared to SL BPN/NX (7.3%) (95% CI 0.2%, 16.8%; p=0.047). In the study, all five participants with overdose (4, accidental; 1 intentional) were in the PWIO SL BPN/NX group. Heroin was involved in the 3 of the 4 cases of accidental overdose. In the study, there were no clinically meaningful differences between the treatments for serious adverse events (SAEs); however, all SAEs in the Infections and Infestations System Organ Class, including abscess (1 limb; 1 subcutaneous), acute hepatitis C (n=1), cellulitis (n=1), localized infection (n=1), osteomyelitis (n=1), pneumonia (n=1), and sepsis (n=1), occurred in the PWIO SL BPN/NX group, suggesting ongoing IV drug use in this group. The retention rate for PWIO was higher in the CAM2038 group (58%) compared to SL BPN/NX group (49%).

Conclusions: Treatment with CAM2038 in PWIO is effective in reducing illicit opioid use and may improve outcomes, decreasing the occurrence of skin, soft tissue and blood bacterial infections, and overdose.

INTRODUCTION

- An estimated 3 million people in the United States aged 15 to 64 are people who inject illicit drugs (PWID)[1]
- PWID are susceptible to serious health hazards including blood-borne diseases and bacterial skin, soft tissue, and blood infections[2]
- Cellulitis and skin or soft tissue abscesses affect up to 32% of PWID at a given time, and are the most common reasons for hospitalization of PWID[2,3]
- An estimated 72.7% of PWID mainly inject opioids (PWIO)[4]
- Injection drug use is associated with treatment attrition and opioid misuse during treatment for OUD[5]
- SL BPN/NX is known to be effective in the treatment of OUD; however, treatment response is typically lower in PWIO[5]

METHODS

- A 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, SL BPN/NX, in buprenorphine initiation and maintenance treatment[6]
- A post-hoc analysis was conducted (intent-to-treat [ITT] population) to assess efficacy of CAM2038 compared with SL BPN/NX in treating PWIO
- Participants randomized 1:1 to SL BPN/NX tablets + placebo SC injections or CAM2038 SC injections + SL placebo tablets
- The study involved four phases: screening, phase 1 (12 weekly visits), phase 2 (3 monthly visits plus 3 unscheduled urine sample visits), and follow-up
- Inclusion criteria: age 18 to 65 years, diagnosed with and seeking treatment for moderate-to-severe OUD, considered to be good candidates for buprenorphine treatment based on medical and psychosocial history, and willing to use reliable contraception
- Exclusion criteria: receiving pharmacotherapy for OUD within 60 days or any investigational drug within 4 weeks; AIDS; chronic pain requiring opioid therapy; pregnancy, lactation, or planned pregnancy; hypersensitivity or allergy to buprenorphine, other opioids, or excipients in CAM2038; use of strong cytochrome P450 3A4 inhibitors (azole antifungals, macrolide antibiotics, or protease inhibitors); recent or current suicidal ideation or behavior; risk for torsades de pointes (heart failure, hypokalemia, or family history of long QT syndrome); electrocardiogram with Fridericia formula QTc > 450 milliseconds in men and > 470 milliseconds in women; aspartate aminotransferase or alanine aminotransferase levels 3-fold higher than the upper limits of the reference range; total bilirubin or creatinine level 1.5-fold higher than the upper limits of the reference range; or pending legal action or other factors or conditions that could adversely affect participant safety and adequate adherence
- Assessments:
  - Urine samples collected at all scheduled visits (weekly during Phase 1 and monthly during Phase 2) plus 3 random unscheduled visits during phase 2; missing urine tests were imputed as positive
    - Urine toxicology was conducted using quantitative methods (liquid chromatography-tandem mass spectrometry [LC/MS-MS])
  - Participant self-reports using a timeline follow-back interview at all visits
  - Other outcomes: time to first illicit opioid use, percentage of illicit opioid use by month, and cumulative percentage of negative urine results at 6 months; craving and withdrawal; and safety based on adverse event (AE) reporting
    - Self-reported opioid craving was measured with unipolar “desire-to-use” and “need-to-use” 100-mm visual analogue scales (VAS, range 0 [none] to 100 [strongest possible])
    - Opioid withdrawal was measured at screening, day 1, and at all scheduled visits by the Subjective Opioid Withdrawal Scale (SOWS) and Clinical Opioid Withdrawal Scale (COWS)
- Adverse events were coded by primary system organ class (SOC) and preferred term according to MedDRA version 18, and summarized by number and percent of subjects in each primary SOC and preferred term
- The prespecified primary endpoint was responder rate (RR), with a responder defined as having no evidence of illicit opioid use (negative urine test for opioids supported by self-report of no illicit use) at ≥8 of 10 pre-specified time points over weeks 9–24; 2 were required at week 12 and during month 6 (weeks 21-24)
- Continuous data were summarized using descriptive statistics; categorical data were summarized as frequencies and percentages (chi-square for RR; analysis of variance (ANOVA) for mean urine toxicology; Wilcoxon for CDF)

RESULTS

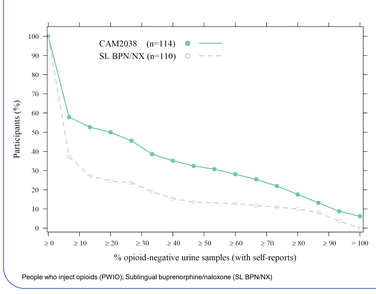
Table 1. Demographics and clinical characteristics of PWIO (n=224) at baseline

Category	CAM2038 N = 114	SL BPN/NX N = 110	All participants N = 224
Age, mean (SD), y	37.32 (11.65)	37.15 (11.54)	37.24 (11.57)
Male, No. (%)	62 (54.4)	73 (66.4)	135 (60.3)
White, No. (%)	90 (78.9)	91 (82.7)	181 (80.8)
BMI, mean (SD), kg/m²	25.01 (4.89)	25.41 (4.97)	25.21 (4.92)
Employed full or part time, No. (%)	34 (29.8)	28 (25.5)	62 (27.7)
Education level, No. (%)			
College or university degree (2 or 4 year)/ Graduate	8 (7.0)	12 (10.9)	20 (8.9)
Did not complete high school	20 (17.5)	25 (22.7)	45 (20.1)
High school diploma or GED	43 (37.7)	40 (36.4)	83 (37.1)
Some college or certificate program	43 (37.7)	33 (30.0)	76 (33.9)
History of any arrest, No. (%)	80 (70.2)	86 (78.2)	166 (74.1)
Duration since OUD diagnosis, mean (SD), y	3.06 (5.29)	2.76 (3.54)	2.95 (4.66)
Heroin primary opioid of use, No. (%)	97 (85.1)	95 (86.4)	192 (85.7)
Utox positive for Fentanyl at screening, No. (%)	36 (31.6)	24 (21.8)	60 (26.8)
Nonopioid drug use at screening, No (%):			
Methamphetamine	21 (18.4)	23 (20.9)	44 (19.6)
Benzodiazepine	12 (10.5)	13 (11.8)	25 (11.2)
Marijuana	28 (24.6)	32 (29.1)	60 (26.8)
Cocaine	34 (29.8)	33 (30.0)	67 (29.9)
Hepatitis C antibody positive at screening, No. (%)	72 (63.2)	73 (66.4)	145 (64.7)
Medical history of depression, No. (%)	14 (12.3)	17 (15.5)	31 (13.8)
COWS, mean (SD)	11.81 (5.27)	12.06 (6.58)	11.93 (5.94)
SOWS, mean (SD)	30.54 (14.53)	31.23 (17.28)	30.88 (15.91)
Desire to use VAS (SD)	76.78 (25.48)	77.71 (25.76)	77.24 (25.57)
Need to use VAS (SD)	74.38 (26.92)	76.43 (25.90)	75.39 (26.38)

Body mass index (BMI); Clinical Opioid withdrawal scale (COWS); Graduate equivalency exam (GED); Standard deviation (SD); Subjective Opioid withdrawal scale (SOWS); Visual analog scale (VAS); Sublingual buprenorphine/naloxone (SL BPN/NX)

- Of the 428 participants randomized, 224 (52.33%) identified injection as the preferred route of illicit opioid use at baseline
- Demographics and clinical characteristics were similar between treatment groups in PWIO
- The percentage of responders for PWIO was higher in the CAM2038 group (15.8%) compared to SL BPN/NX (7.3%; 95% CI 0.2%, 16.8%; p= 0.047)
- The retention rate in study was 55% in the CAM2038 group compared to 49% for the SL BPN/NX group for PWIO

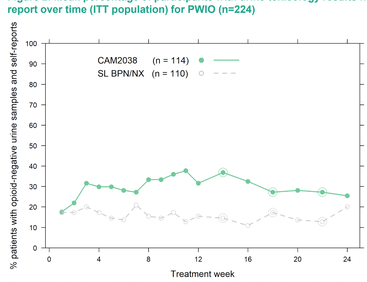
Figure 1: Cumulative distribution function (CDF) of percentage of illicit opioid-negative urine samples confirmed by self-report for treatment weeks 4 to 24 for PWIO (n=224)



- p <0.001 (Wilcoxon; superiority)
- Median (weeks 4 to 24)
  - CAM2038: 16.7%
  - SL BPN/NX: 0
- LS Mean (SE) (weeks 4 to 24)
  - CAM2038: 30.9% (3.3)
  - SL BPN/NX:15.4% (2.7)

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

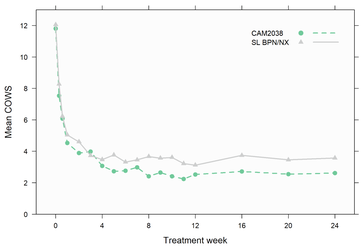
Figure 2. Mean percentage of participants with urine toxicology results negative for illicit opioids supported by self-report over time (ITT population) for PWIO (n=224)



- The mean percentage of urine samples negative for illicit opioids supported by self-reports was higher in the CAM2038 group (29.7%) relative to SL BPN/NX group (15.9%), a 13.9% difference (95% CI, 4.7%, 23.0%; p=0.003; superiority [ANOVA])

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

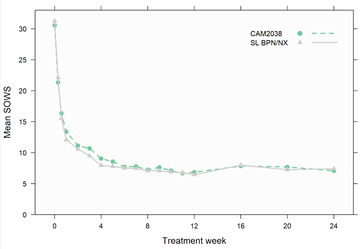
Figure 3. Clinical Opioid Withdrawal Scale (COWS) scores over time in PWIO (n=224)



- In both groups, opioid withdrawal, as evaluated by COWS, was suppressed from day 1 and throughout the study, including during transitions from weekly to monthly injections, without significant group differences

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

Figure 4. Subjective ratings of withdrawal (SOWS) over time in PWIO (n=224)

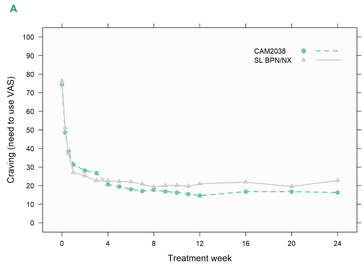


- In both groups, opioid withdrawal, as evaluated by SOWS, was suppressed from day 1 and throughout the study, including during transitions from weekly to monthly injections, without significant group differences

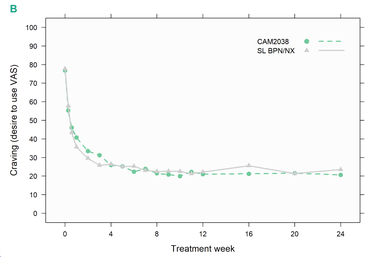
People who inject opioids (PWIO); Sublingual buprenorphine/naloxone (SL BPN/NX)

Figure 5. Mean craving assessed by A) need to use and B) desire to use VAS by treatment week and treatment group in PWIO (n=224)

A



B



- In both groups, opioid craving was suppressed at treatment initiation on day 1 and throughout the study, including during transitions from weekly to monthly injections, without significant group differences
- Desire to Use and Need to Use (opioid cravings) was assessed using unipolar 100 mm VAS (“Since your last scheduled assessment visit, indicate your worst or strongest desire/need to use opioids, where 0 = No desire to use and 100 mm = Strongest possible desire, and from 0 = No need to use and 100 mm = Strongest possible need, respectively”)

People who inject opioids (PWIO); Sublingual buprenorphine/naloxone (SL BPN/NX); Visual analog scale (VAS)

Table 2. Summary of Non-Fatal Serious Adverse Events in PWIO (Safety Population)

System Organ Class/Preferred Term	CAM2038 N=114 n (%)	SL BPN/NX N=110 n (%)	Total N=224 n (%)
Infections and infestations	0	8 (7.3)	8 (3.6)
Abscess limb	0	1 (0.9)	1 (0.4)
Acute hepatitis C	0	1 (0.9)	1 (0.4)
Cellulitis	0	1 (0.9)	1 (0.4)
Localised infection	0	1 (0.9)	1 (0.4)
Osteomyelitis	0	1 (0.9)	1 (0.4)
Pneumonia	0	1 (0.9)	1 (0.4)
Sepsis	0	1 (0.9)	1 (0.4)
Subcutaneous abscess	0	1 (0.9)	1 (0.4)
Injury, poisoning and procedural complications	0	4 (3.6)	5 (2.2)
Accidental overdose	0	3 (2.7)	3 (1.3)
Intentional overdose	0	1 (0.9)	1 (0.4)
Psychiatric disorders	0	3 (2.7)	2 (0.9)
Bipolar disorder	0	1 (0.9)	1 (0.4)
Substance-induced mood disorder	0	1 (0.9)	1 (0.4)
Suicidal ideation	0	1 (0.9)	2 (0.9)
Congenital, familial and genetic	0	1 (0.9)	1 (0.4)
Haemophilia	0	1 (0.9)	1 (0.4)
Gastrointestinal disorders	1 (0.9)	0	1 (0.4)
Vomiting	1 (0.9)	0	1 (0.4)
Pregnancy, puerperium and perinatal conditions	1 (0.9)	0	1 (0.4)
Abortion spontaneous	1 (0.9)	0	1 (0.4)

People who inject opioids (PWIO); Sublingual buprenorphine/naloxone (SL BPN/NX); Serious adverse event (SAE); System organ class (SOC)

- All five participants with overdose (n = 4 accidental; n = 1 intentional) were in the SL BPN/NX group; heroin was involved in the 3 of the 4 cases of accidental overdose; 1 overdose occurred in the context of withdrawal after being jailed without study medication
- There were no clinically meaningful differences between the treatments for SAEs; however, all SAEs in the Infections and Infestations System Organ Class, including abscess (n = 1, limb; n = 1 subcutaneous), acute hepatitis C (n = 1), cellulitis (n = 1), localized infection (n = 1), osteomyelitis (n = 1), pneumonia (n = 1), and sepsis (n = 1), occurred in the SL BPN/NX group, suggesting ongoing IV drug use
- With the exception of injection site treatment-emergent adverse events, the safety profile observed with CAM2038 was consistent with the known safety profile of SL BPN; no unexpected adverse events were observed

CONCLUSIONS

- Treatment with CAM2038 may reduce the likelihood of illicit opioid use in PWIO. The results of this subgroup analysis also suggest reductions in the occurrence of skin, soft tissue, and blood bacterial infections and risk of overdose compared with current standard of treatment with daily SL BPN/NX in PWIO.
- Observed reduction in illicit opioid use in the CAM2038 group may be related to steady delivery of buprenorphine provided by the long-acting injection.
- CAM2038 demonstrated sustained opioid withdrawal and craving suppression from day 1 and through maintenance treatment, including during transition from weekly to monthly injections, in PWIO.

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