Long-term safety, tolerability and effectiveness of weekly and monthly buprenorphine depot (CAM2038) for opioid use disorder

Adrian Dunlop[1], Michael Frost[2], Nicholas Lintzeris[3], Edward Nunes[4], Genie Bailey[5], Jakob Billeskov Jansen[6], Lars Chemnitz Frey[7], Bernd Weber[8], John Strang[9], Sonnie Kim[10], Fredrik Tiberg[11]

1. University of Newcastle, NSW Australia; Hunter New England Local Health District, NSW Australia; 2. The Frost Medical Group, Philadelphia, PA, USA; 3. University of Sydney, NSW Australia; Sydney South East Local Health District, NSW Australia; 4. New York State Psychiatric Institute and Columbia University Department of Psychiatry, New York, NY, USA; 5. Warren Alpert Medical School of Brown University, Providence, RI, USA; 6. Center For Misbrugsbehandling, Aarhus, Denmark; 7. Behandlingscenter Odense, Odense, Denmark; 8. Praxiszentrum Friedrichsplatz, Kassel, Germany; 9. Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK; 10. Braeburn Pharmaceuticals, Princeton, NJ, USA; 11. Camurus AB, Lund, Sweden

Background

While buprenorphine is an efficacious treatment for opioid use disorder (OUD), daily oral/transmucosal preparations may be associated with poor adherence and extra-medical use including diversion and injection. Long acting preparations of opioid medications have the potential to improve adherence and reduce illicit opioid use.

Research Question(s)

To demonstrate long-term safety and local tolerability and evaluate efficacy of the depot buprenorphine formulation CAM2038 in adults with moderate-to-severe opioid use disorder. Weekly and monthly buprenorphine depots may improve treatment adherence and outcomes and reduce diversion and illicit opioid use compared with daily medications.

Methods

This multinational open-label, flexible dosing study conducted in Europe, North America and Australia enrolled participants either seeking or currently in OUD treatment, to individualised outpatient treatment with CAM2038. The study included screening, 48-weeks of treatment and 4 weeks of follow-up. Safety and local tolerability, urinalysis, self-report of drug use, craving, withdrawal and other outcome measures were collected.

Results

A total of 227 participants were enrolled and dosed with CAM2038 of which 73.6% completed the study treatment period (**Table 1**). Treatment retention over time is shown in **Figure 1**.

TABLE 1. Demographics and baseline clinical characteristics (Overall Safety Population)

Characteristic	Transferred from SL BPN treatment N = 190	New to BPN treatment N = 37	Overall N = 227
Age, y, mean (SD)	41.3 (9.64)	41.8 (9.41)	41.4 (9.59)
Sex			
Male	119 (62.6)	24 (64.9)	143 (63.0)
Female	71 (37.4)	13 (35.1)	84 (37.0)
Race			
White	183 (96.3)	20 (54.1)	203 (89.4)
Black or African American	3 (1.6)	17 (45.9)	20 (8.8)
Other	4 (2.1)	0 (0)	4 (1.8)
BMI, kg/m^2, mean (SD)	26.7 (5.84)	25.3 (5.33)	26.5 (5.77)
Region			
Australia	23 (12.1)	1 (2.7)	24 (10.6)
Europe	76 (40.0)	0 (0)	76 (33.5)
United States	91 (47.9)	36 (97.3)	127 (55.9)
Employment status			
Employed	106 (55.8)	13 (35.1)	119 (52.4)
Unemployed	77 (40.5)	23 (62.2)	100 (44.1)
Other	7 (3.7)	1 (2.7)	8 (3.5)
Marital status			
Married	59 (31.1)	6 (16.2)	65 (28.6)
Single	102 (53.7)	30 (81.1)	132 (58.1)
Other	29 (15.3)	1 (2.7)	30 (13.2)
Residential status			
Own	55 (28.9)	2 (5.4)	57 (25.1)
Rent	121 (63.7)	33 (89.2)	154 (67.8)
Other	14 (7.4)	2 (5.4)	16 (7.0)
Arrest and conviction history			
Previously arrested	48 (25.3)	10 (27.0)	58 (25.6)
Felony conviction	15 (7.9)	11 (29.7)	26 (11.5)
Misdemeanour conviction	18 (9.5)	5 (13.5)	23 (10.1)
Neither	108 (56.8)	11 (29.7)	119 (52.4)
Substance abuse history			
Opioid use disorder (DSM-5) diagnosis	157 (82.6)	37 (100.0)	194 (85.5)
Time to first opioid abuse	14.7 (8.48)	15.7 (8.98)	14.8 (8.55)
Time to first diagnosis	9.8 (7.60)	10.0 (8.60)	9.8 (7.75)
Heroin as primary opioid of use	97 (51.1)	37 (100.0)	134 (59.0)
Baseline withdrawal and cravings			
COWS at baseline	2.0 (2.7)	10.6 (3.7)	3.4 (4.3)
SOWS at baseline	4.7 (8.1)	27.1 (15.3)	8.3 (12.7)
Desire to use VAS at baseline	11.7 (24.2)	74.8 (24.8)	22.0 (33.7)
Need to use VAS at baseline	11.7 (23.8)	76.3 (24.9)	22.3 (33.8)

Unless otherwise noted, data presented as n (%).
BMI, body mass index; BPN, buprenorphine; COWS, clinical opioid withdrawal scale (0–48); DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; SD, standard deviation; SL BPN, sublingual buprenorphine; SOWS, subjective opioid withdrawal scale (0–64); VAS, visual analogue scale (0–100 mm).

TABLE 2. Summary of treatment-emergent adverse events

	Overall Safety Population		
Category	**Transferred from SL BPN N = 190**	**New to BPN treatment N = 37**	**Overall N = 227**
A least 1 TEAE	131 (68.9)	12 (32.4)	143 (63.0)
At least 1 drug-related TEAE	58 (30.5)	2 (5.4)	60 (26.4)
Injection site TEAE	43 (22.6)	2 (5.4)	45 (19.8)
Non-injection site TEAE	23 (12.1)	1 (2.7)	24 (10.6)
At least 1 severe TEAE	13 (6.8)	2 (5.4)	15 (6.6)
Deaths	0 (0)	0 (0)	0 (0)
At least 1 SAE	10 (5.3)	2 (5.4)	12 (5.3)
At least 1 drug-related SAE	0 (0)	0 (0)	0 (0)
Hospitalisations	9 (4.7)	1 (2.7)	10 (4.4)
TEAEs leading to discontinuations	3 (1.6)	0 (0)	3 (1.3)
TEAEs in ≥5% of participants			
Nasopharyngitis	17 (8.9)	1 (2.7)	18 (7.9)
Urinary tract infection	9 (4.7)	3 (8.1)	12 (5.3)
Gastrointestinal disorders	42 (22.1)	2 (5.4)	44 (19.4)
Nausea	16 (8.4)	0 (0)	16 (7.0)
Vomiting	12 (6.3)	0 (0)	12 (5.3)
Diarrhoea	8 (4.2)	1 (2.7)	9 (4.0)
Headache	18 (9.5)	0 (0)	18 (7.9)
Injection site pain	33 (17.4)	2 (5.4)	35 (15.4)
Injection site swelling	25 (13.2)	2 (5.4)	27 (11.9)
Injection site erythema	20 (10.5)	1 (2.7)	21 (9.3)

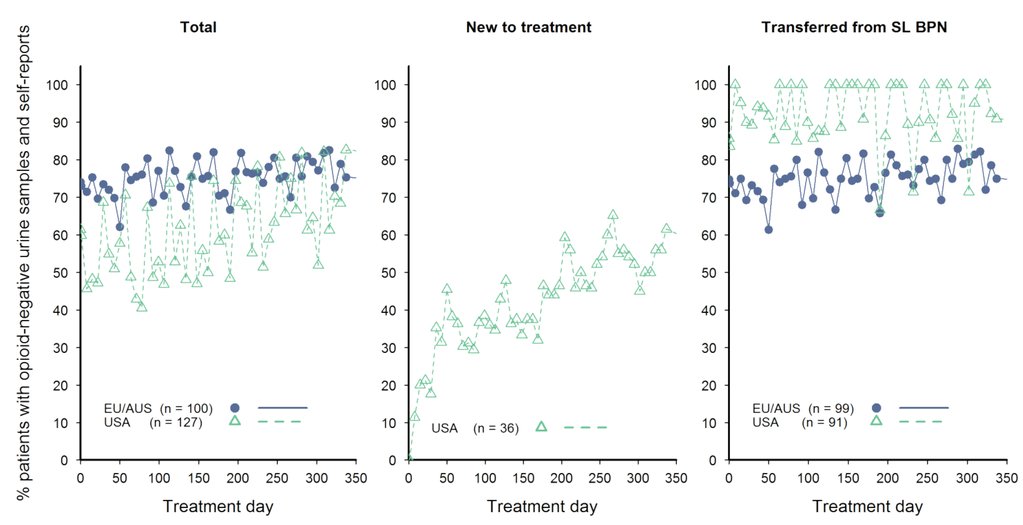
Data presented as n (%).
BPN, buprenorphine; SL BPN, sublingual buprenorphine; TEAE, treatment-emergent adverse event; SAE, serious adverse event.

FIGURE 1. Retention in treatment by region with EU and AUS combined

Overall, 63.0% experienced any treatment emergent adverse event (TEAE), mostly mild to moderate intensity. No serious TEAEs (5.3%) were considered related to study drug. The safety profile of CAM2038 was generally consistent with the known safety profile of buprenorphine, except for mild to moderate injection site reactions (19.8%)(**Table 2**).

Efficacy was generally maintained or improved over the study with a pronounced improvement for new to treatment patients (**Figure 2**). Across the study, 76% of participant assessments showed no illicit opioid use. Cravings and withdrawal were well controlled with need to use VAS<9 mm (scale: 0-100 mm), and COWS<2 (scale 0-48) from Month 2 to 48. Data from the European sites will be presented as a sub-group analysis and compared to results from North American and Australia.

FIGURE 2. Illicit Opioid Use With Self-Reports (not imputed) by region with EU and AUS combined



Conclusions

CAM2038 demonstrated safety, tolerability across 48-weeks and may be an effective OUD treatment and provide an additional option for people who use opioids and do not respond to sublingual buprenorphine.