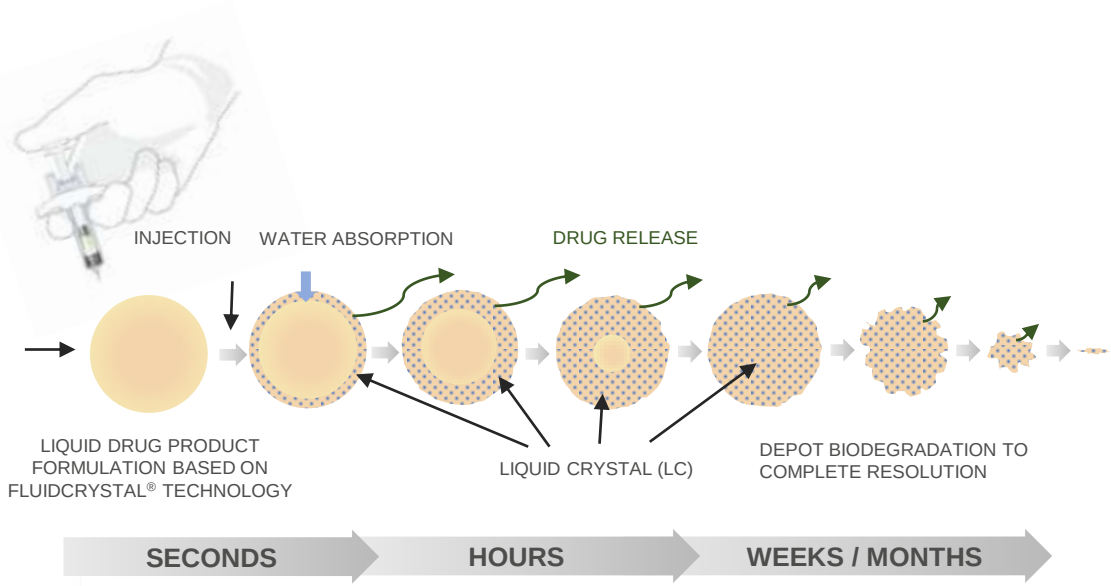
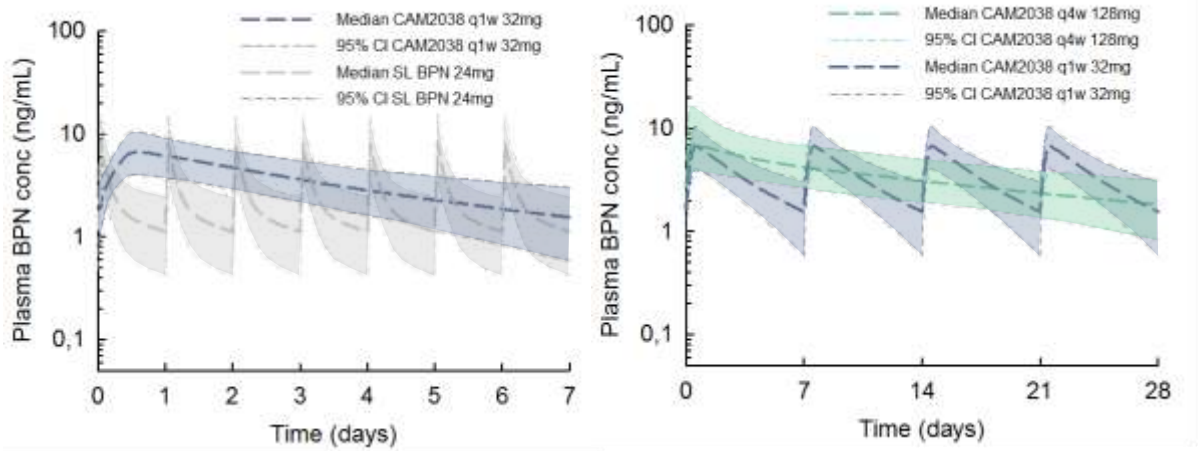
Buvidal®(buprénorphine á action prolongée): un DEBUT dans les traitements de l'addiction aux opiacés

Dr. Fredrik Tiberg, CEO and Head of R&D
20 October 2021
ATHS Biarritz

Subcutaneous depot buprenorphine injection: Buvidal® (CAM2038)

- Ready-for-use in pre-filled syringe (0.16–0.64 mL)
- Stored at room temperature
- Subcutaneous injection by HCP; multiple sites (buttock, abdomen, upper arm, thigh)





Flexible dosing options:

- Weekly: 8 mg, 16 mg, 24 mg, 32 mg
- Monthly: 64 mg, 96 mg, 128 mg, 160 mg

Source. 1. Tiberg F et al. Chem Lett 2012; 41: 1090-1092; 2. Tiberg F et al. J. Drug Deliv Sci Tech. 2011; 21: 101-109. 3. EPAR Dec 2018 EMEA/H/C/004651/0000 https://www.ema.europa.eu/documents/assessment-report/buvidal-epar-public-assessment-report_en.pdf

Background: evidence base for depot buprenorphine

- Effective suppression of withdrawal and cravings[1,2,3]
- Blockade of opioid effects[2]
- Pharmacokinetic profiles for weekly and monthly dosing[4]
- Non-inferior and superior efficacy for illicit opioid use demonstrated in pivotal double-blind Phase 3 study versus standard daily SL BPN/NX in new to treatment patients[1]
- Retention rates high in both new to treatment patients and patients switched from SL BPN[1,3]
- Safety profile comparable to SL BPN except for mild to moderate injection site reactions[1,2,3]

SL BPN/NX, sublingual buprenorphine/naloxone

Source: 1. Lofwall et al. JAMA Int. Med. 2018;178(6); 764-773; 2. Walsh et al, JAMA Psychiatry 2017;74(9):894-902; 3. Frost M et al. Addiction. 2019;114:1416-1426; 4. Albayaty M, et al, Adv Ther. 2017 34(2):560-575

DEBUT – first RCT comparing PROs of treatment with weekly and monthly depot BPN to daily SL BPN

The Depot Evaluation–Buprenorphine Utilization Trial (DEBUT)


JAMA Network Open

Original Investigation | Substance Use and Addiction

Patient-Reported Outcomes of Treatment of Opioid Dependence With Weekly and Monthly Subcutaneous Depot vs Daily Sublingual Buprenorphine
A Randomized Clinical Trial

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PRO, patient reported outcome; RCT, randomised clinical trial; BPN subcutaneous buprenorphine; SL BPN, sublingual buprenorphine

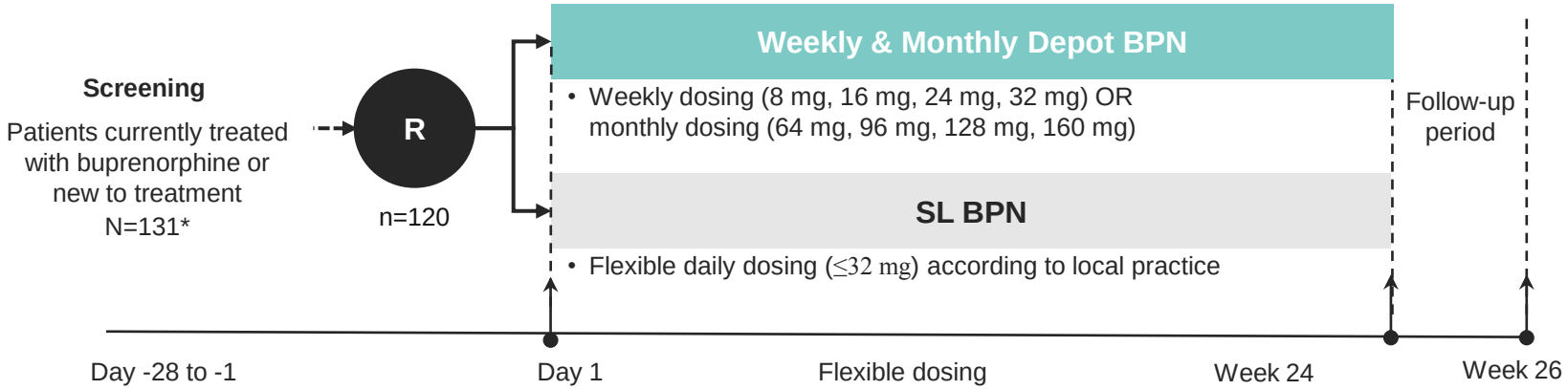
Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

Study design

Randomised, multi-site, open-label, active-controlled study of depot BPN vs standard of care in 120 adult outpatients with opioid dependence to compare patient reported outcomes (PROs)

Primary endpoint: patient reported TSQM global satisfaction score

Secondary endpoints (selected): TSQM effectiveness, convenience and side effects score and other PRO measures of patient satisfaction, treatment burden, quality of life, burden of treatment, opioid related behaviors, and traditional measures



*All patients randomised and receiving treatment in the study had previously received SL BPN. In total, 11 patients were excluded as they did not meet inclusion criteria. One participant (0.8%) who had been randomised to receive SL BPN withdrew consent and did not receive study treatment.

Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

BPN, buprenorphine; R, randomised; SL BPN, sublingual buprenorphine; TSQM, treatment satisfaction questionnaire for medication

Randomisation and treatment

Population

120 adults aged ≥18 years with opioid dependence
(mean age 44.4 years, SD 10.5 years)

Setting

6 out-patient clinical sites in Australia

Intervention

Randomised (n=120), received treatment (n=119)

Depot BPN (n=60)
Weekly or monthly dose
(maximum dose, 32 mg weekly or 160 mg monthly)

SL BPN SoC (n=59)
Daily dose
(maximum daily dose, 32 mg)

BPN, buprenorphine; SD, standard deviation; SL BPN SoC, sublingual buprenorphine standard of care

Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

Demographics and baseline characteristics in DEBUT

Characteristics	Depot BPN (n=60)	SL BPN (n=59)
Age, years, mean (SD)	43.6 (10.4)	45.3 (10.6)
Sex (Male), n (%)	34 (56.7%)	36 (61.0%)
Race (White), n (%)	51 (85.0%)	51 (86.4%)
BMI, mean (SD)	26.7 (6.5)	28.2 (6.0)
Employed, n (%)	14 (23.3%)	13 (22.0%)
Medical history		
Hepatitis C, n (%)	34 (56.7%)	21 (35.6%)
Depression, n (%)	29 (48.3%)	36 (61.0%)
Baseline withdrawal and cravings, mean (SD)		
Opioid craving VAS at baseline	21.5 (23.7)	30.7 (29.0)
COWS at baseline	1.8 (2.9)	2.0 (2.4)

BMI, body mass index; BPN, buprenorphine; COWS, Clinical Opiate Withdrawal Scale; SD, standard deviation; SL BPN, sublingual buprenorphine; VAS, visual analog scale.

Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

Demographics and baseline characteristics in DEBUT

Characteristics	Depot BPN (n=60)	SL BPN (n=59)
Opioid dependence history		
Years from first illicit use of opioid to randomization, mean (SD)	19.7 (12.5)	19.0 (12.8)
Heroin primary opioid used, n (%)	44 (73.3%)	33 (55.0%)
Injection use, n (%)	41 (68.3%)	36 (60.0%)
Age when first used heroin, years, mean (SD)	22.2 (7.5)	21.9 (6.6)
Drug use by UDS with self-reports at screening		
Amphetamine, n (%)	24 (40.0%)	11 (18.6%)
Cocaine, n (%)	4 (6.7%)	4 (6.8%)
Cannabinoids, n (%)	24 (40.0%)	18 (30.5%)
Benzodiazepines, n (%)	18 (30.0%)	22 (37.3%)

BPN, buprenorphine; SD, standard deviation; SL BPN, sublingual buprenorphine; UDS, urine drug screen.

Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

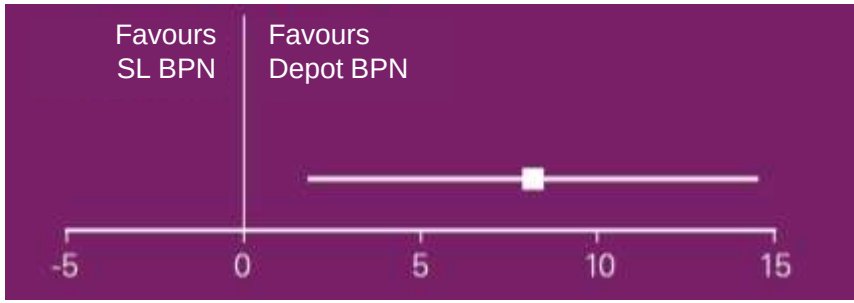
Superior patient reported global treatment satisfaction with depot BPN vs SL BPN

Primary outcome

The difference in global treatment satisfaction score, as measured by TSQM at Week 24

Findings

Mean TSQM global satisfaction score at Week 24 was significantly higher among participants who received depot BPN compared to those who received SL BPN (difference 8.2; 95% CI: 1.7–14.6; p=0.01)



Between-group difference in TSQM global satisfaction score

BPN, buprenorphine; SL BPN, sublingual buprenorphine

Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

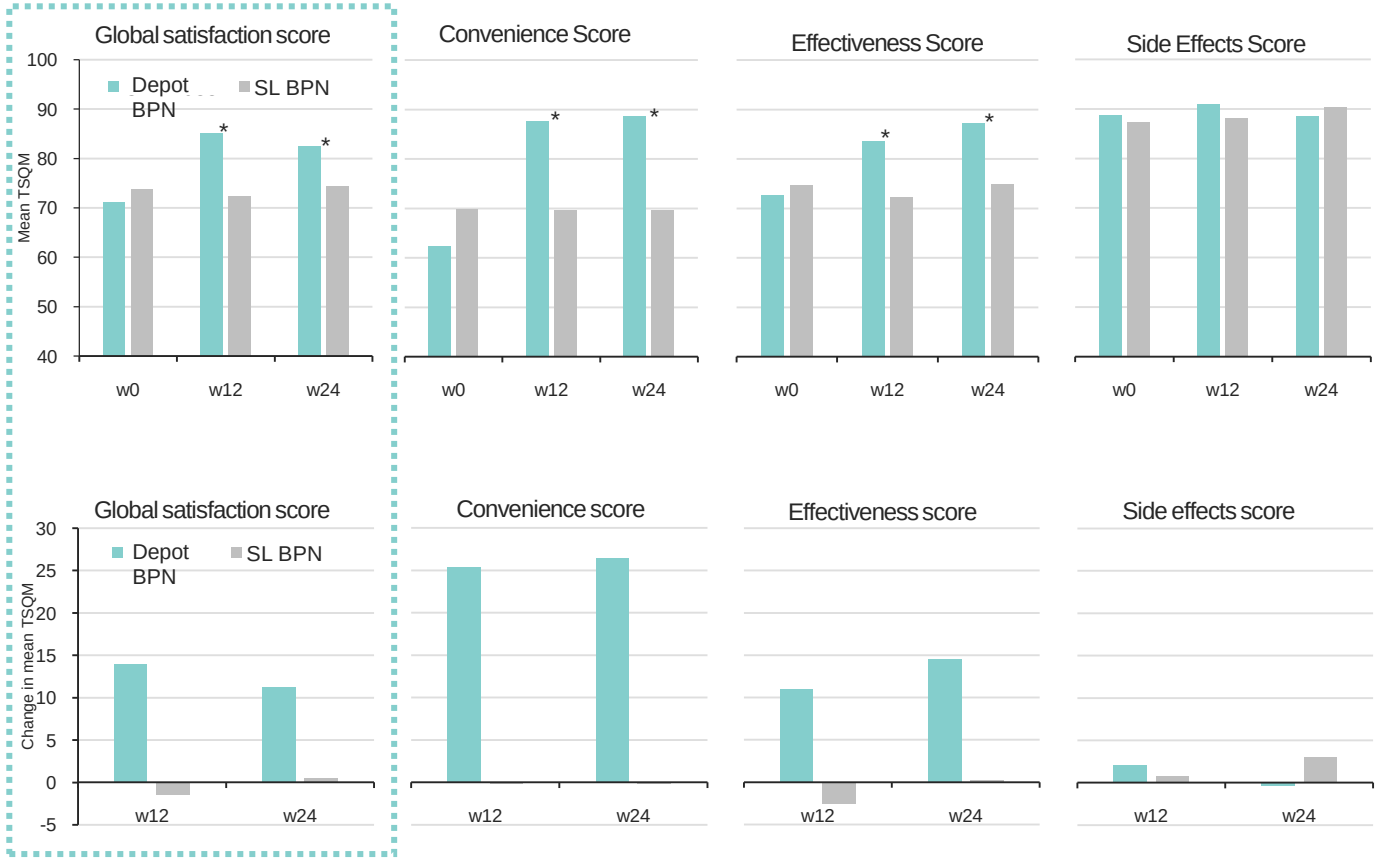
High patient reported treatment satisfaction with depot BPN vs SL BPN

Primary endpoint

Superiority for depot BPN TSQM global satisfaction score at Week 24; 82.5% vs. 74.3%, p=0.01

Absolute TSQM scores (higher is better)

Change from baseline (higher is better)



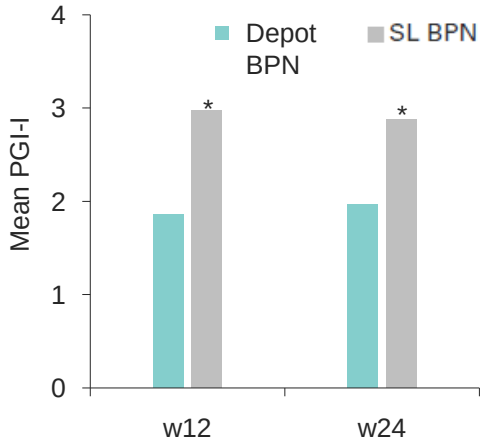
Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

BPN, buprenorphine; SL BPN, sublingual buprenorphine; TSQM, Treatment Satisfaction Questionnaire for Medication.

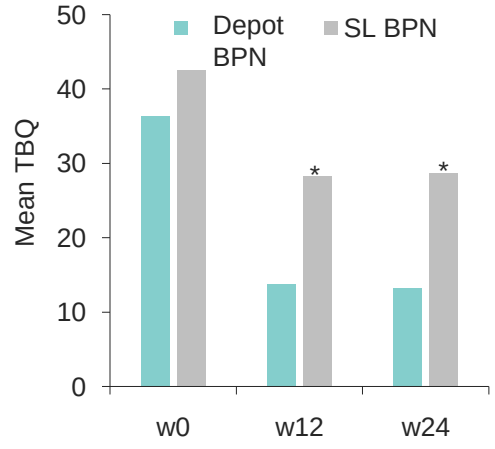
Reduced treatment burden and improved quality of life with depot BPN vs. SL BPN

Secondary outcomes: Improvements for patient global impression of improvement (PGI-I), treatment burden (TBQ), and quality of life medication domain (OSTQoL OST domain)*

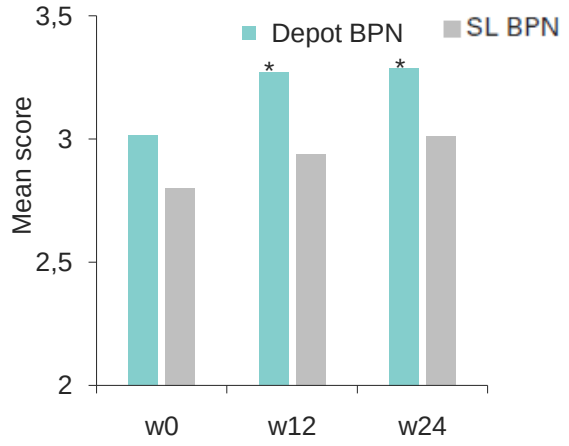
Patient Global Impression of Improvement
(PGI-I) (lower is better)



Treatment Burden Questionnaire
(TBQ) (lower is better)



Opioid Substitution Treatment Quality of Life
(OSTQoL) - OST domain (higher better)



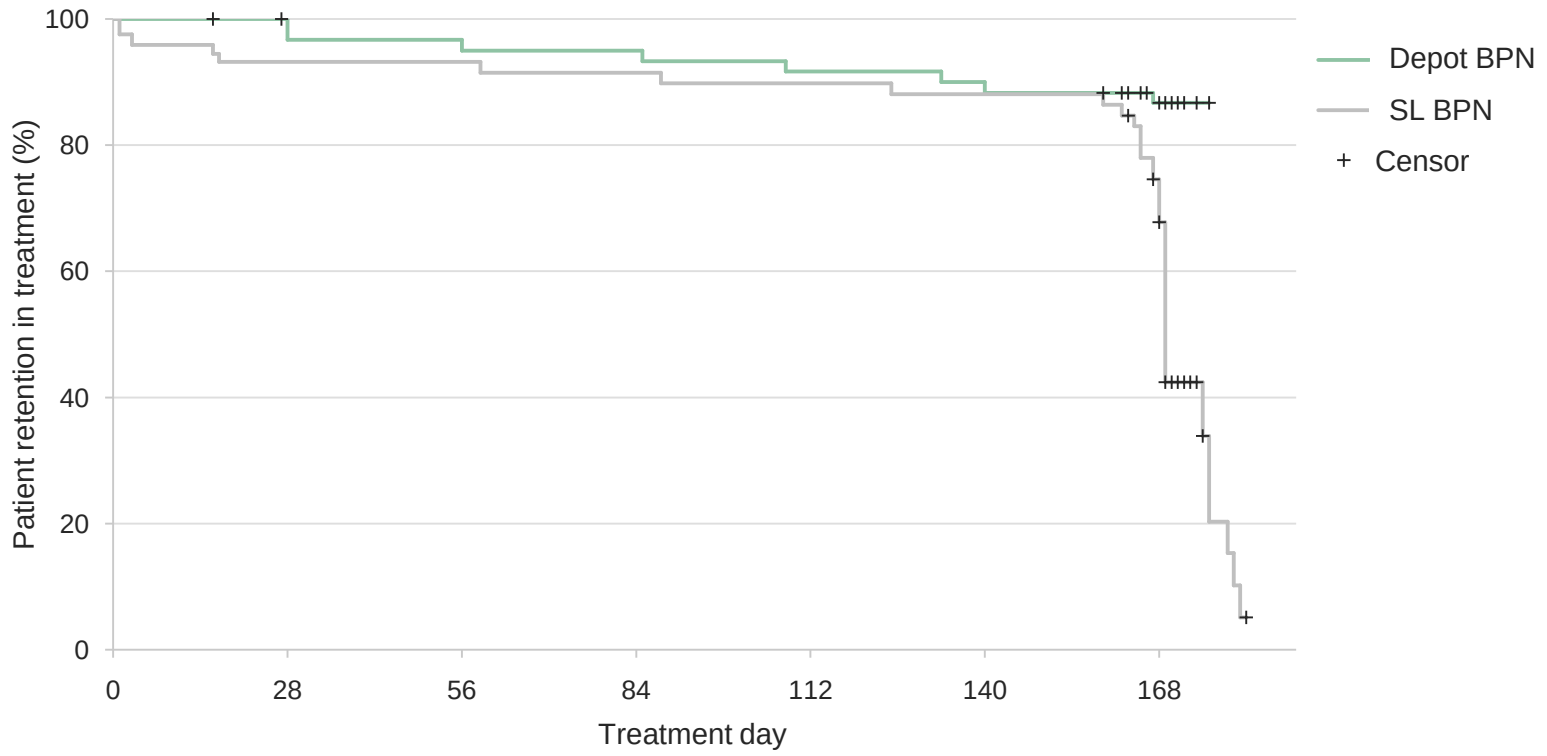
*These secondary outcomes were selected among other PRO instruments as being mostly related to satisfaction with treatment.

BPN, buprenorphine; PRO, patient reported outcome; SL BPN, sublingual buprenorphine.

Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

Study retention

High study retention in both groups with no significant differences[1]



[1]*Patients in both groups were offered treatment with weekly and monthly depot BPN after completing the study; Lintzeris N, et al. Results of the DEBUT study presented at The College on Problems of Drug Dependence (CPDD), virtual meeting, June 22–24, 2020.*

Depot BPN individualised doses in the study

Regimen

Weekly Depot BPN (maximum doses achieved)	N=29 (48%)
Mean (SD) (mg)	23.2 (9.2)
8 mg	5 (8.3%)
16 mg	5 (8.3%)
24 mg	7 (11.7%)
32 mg	12 (20.0%)
Monthly Depot BPN (maximum doses achieved)	N=60
Mean (SD) (mg)	116.8 (31.63)
64 mg	9 (15.0%)
96 mg	16 (26.7%)
128 mg	22 (36.7%)
160 mg	13 (21.7%)
Number participants receiving supplemental doses: Doses occurred early in treatment (none > 20 weeks)	20/60 (33%) 15 clients x 1 supplemental dose 1 client x 4 doses

Sublingual buprenorphine film: From total supervised dosing to ‘up to 6 takeaway doses/week’ as per routine care; flexible doses up to 32 mg daily dose. Mean dose = 15.6±7.6mg. Dosing at clinics / community pharmacies and all dosing was free to clients during study.

BPN, buprenorphine; SD, standard deviation

Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

Safety and tolerability consistent with safety profiles of BPN and Buvidal*

Characteristic	Patients, No.		
	Depot BPN (n=60)	SL BPN (n=59)	Overall (n=119)
TEAEs	54 (90.0%)	49 (83.1%)	103 (86.6%)
Drug-related ADRs	39 (65.0%)	12 (20.3%)	51 (42.9%)
SAEs	9 (15.0%)	9 (15.3%)	18 (15.1%)
Serious drug-related ADRs	1 (1.7%)	0	1 (0.8%)
AEs or SAEs leading to withdrawal of medication	0	0	0
Deaths	0	0	0
Drug overdoses	0	4 (6.8%)	4 (3.4%)
AEs in ≥8% of participants			
Injection site pain	11 (18.3%)	0	11 (9.2%)
Injection site mass	10 (16.7%)	0	10 (8.4%)
Injection site bruising	5 (8.3%)	0	5 (4.2%)
Upper respiratory tract infection	7 (11.7%)	2 (3.4%)	9 (7.6%)
Nausea	5 (8.3%)	2 (3.4%)	7 (5.9%)
Vomiting	5 (8.3%)	2 (3.4%)	7 (5.9%)
Toothache	5 (8.3%)	1 (1.7%)	6 (5.0%)
Arthralgia	5 (8.3%)	4 (6.8%)	9 (7.6%)

*Summary of TEAEs in safety analysis set. Treatment-emergent AEs occurring in more than 5 participants in any treatment group are shown.

ADR, adverse drug reaction; AE, adverse event; BPN, buprenorphine; SAE, serious adverse event; SL BPN, sublingual buprenorphine; TEAE, treatment-emergent adverse event

Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

Conclusions

- Findings of this study
  - Improved patient-reported experience and outcomes with Buvidal vs. SL BPN[1]
    - The study met primary endpoint of superiority: TSQM global satisfactory score at Week 24 (p=0.01)
    - TSQM effectiveness and convenience scores were higher at Week 24 (p<0.001), with no difference in safety domain scores (p=0.61)
    - Improvements for patient global impression of improvement (PGI-I), treatment burden (TBQ), and quality of life measures (OSTQoL OST domain; SF-36 physical domain), and opioid related behaviors in treatment (ORBIT)
    - As expected, based on study design, no significant difference in traditional outcomes
- Importance of prioritising patient reported outcomes/experience in evaluating new treatment approaches[2]
- Study impact
  - Experience of DEBUT study informed development of NSW Clinical Guidelines[3] and training programs

SL BPN, sublingual buprenorphine; TSQM, Treatment Satisfaction Questionnaire for Medication

Source: 1. Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041; 2. Compton & Volkow. JAMA Netw Open. 2021. PMID: 33970262; 3. Lintzeris, Dunlop, Masters. Guidance for depot buprenorphine in the treatment of opioid dependence. NSW Health 2019

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- Authors: Nicholas Lintzeris; Adrian J. Dunlop; Paul S. Haber; Dan I. Lubman; Robert Graham; Sarah Hutchinson; Shalini Arunogiri; Victoria Hayes; Peter Hjelmström; Agneta Svedberg; Stefan Peterson; Fredrik Tiberg
- NSW Drug and Alcohol Clinical Research Improvement Network

EU ABBREVIATED PRESCRIBING INFORMATION

Buvidal® (buprenorphine) prolonged-release solution for injection

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentations: Prolonged-release solution for injection in pre-filled syringes containing buprenorphine for weekly injection (8 mg, 16 mg, 24 mg, 32 mg) or monthly injection (64 mg, 96 mg, 128 mg, 160mg). **Indication:** Treatment of opioid dependence within a framework of medical, social and psychological treatment. Treatment is intended for use in adults and adolescents aged 16 years or over. **Dosage and Administration:** Administration of Buvidal® is restricted to healthcare professionals. Appropriate precautions, such as to conduct patient follow-up visits with clinical monitoring to the patient's needs, should be taken when prescribing and dispensing buprenorphine. Take-home use or self-administration of the product by patients is not allowed. *Precautions to be taken before initiation of treatment:* To avoid precipitating symptoms of withdrawal, treatment with Buvidal® should be started when objective and clear signs of mild to moderate withdrawal are evident. For patients using heroin or short-acting opioids, the initial dose of Buvidal® must not be administered until at least 6 hours after the patient last used opioids. For patients receiving methadone, the methadone dose should be reduced to a maximum of 30 mg/day before starting treatment with Buvidal® which should not be administered until at least 24 hours after the patient last received a methadone dose. Buvidal® may trigger withdrawal symptoms in methadone-dependent patients. *Initiation of treatment in patients not already receiving buprenorphine:* Patients not previously exposed to buprenorphine should receive a sublingual buprenorphine 4 mg dose and be observed for an hour before the first administration of weekly Buvidal® to confirm tolerability to buprenorphine. The recommended starting dose of Buvidal® is 16 mg, with one or two additional 8 mg doses at least 1 day apart, to a target dose of 24 mg or 32 mg during the first treatment week. The recommended dose for the second treatment week is the total dose administered during the week of initiation. Treatment with monthly Buvidal® can be started after treatment initiation with weekly Buvidal®, in accordance with the dose conversion in Table 1 of the full SmPC and once patients have been stabilised on weekly treatment (four weeks or more, where practical). *Switching from sublingual buprenorphine products to Buvidal®:* Patients treated with sublingual buprenorphine may be switched directly to weekly or monthly Buvidal®, starting on the day after the last daily buprenorphine sublingual treatment dose in accordance with the dosing recommendations in the full SmPC. Patients may be switched from sublingual buprenorphine 26-32 mg directly to monthly Buvidal 160 mg with close monitoring during the dosing period after the switch. *Maintenance treatment and dose adjustments:* Buvidal® can be administered weekly or monthly. Doses may be increased or decreased and patients can be switched between weekly and monthly products according to individual patient's needs and treating physician's clinical judgement as per recommendations in the full SmPC. Following switching, patients may need closer monitoring. Assessment of long-term treatment is based on 48-week data. *Supplemental dosing:* A maximum of one supplemental Buvidal® 8 mg dose may be administered at an unscheduled visit between regular weekly and monthly doses, based on individual patient's temporary needs. The maximum dose per week for patients who are on weekly Buvidal® treatment is 32 mg with an additional 8 mg dose. The maximum dose per month for patients who are on monthly Buvidal® treatment is 160 mg. *Missed doses:* To avoid missed doses, the weekly dose may be administered up to 2 days before or after the weekly time point, and the monthly dose may be administered up to 1 week before or after the monthly time point. If a dose is missed, the next dose should be administered as soon as practically possible. *Termination of treatment:* If Buvidal® treatment is discontinued, its prolonged-release characteristics and any withdrawal symptoms experienced by the patient must be considered. If the patient is switched to treatment with sublingual buprenorphine, this should be done one week after the last weekly dose or one month after the last monthly dose of Buvidal® according to the recommendations in the full SmPC. **Method of administration:** Buvidal® is intended for subcutaneous administration only. It should be injected slowly and completely into the subcutaneous tissue of different areas (buttock, thigh, abdomen, or upper arm), provided there is enough subcutaneous tissue. Each area can have multiple injection sites. A minimum of 8 weeks should be left before re-injecting a previously used injection site with the weekly dose. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Severe respiratory insufficiency. Severe hepatic impairment. Acute alcoholism or *delirium tremens*. **Special warnings and precautions for use:** Care must be taken to avoid inadvertent injection of Buvidal®. The dose must not be administered intravascularly (intravenously), intramuscularly or intradermally. Intravascular such as intravenous injection would present a risk of serious harm as Buvidal forms a solid mass upon contact with body fluids, which potentially could cause blood vessel injury, occlusion, or thromboembolic events. To minimise the risk of misuse, abuse or diversion, appropriate precautions should be taken when prescribing and dispensing buprenorphine. Healthcare professionals should administer Buvidal directly to the patient. Take-home use or self-administration of the product by patients is not allowed. Any attempts to remove the depot should be monitored throughout treatment. The prolonged-release properties of the product should be considered during treatment including initiation and termination. In particular, patients with concomitant medicinal products and/or co-morbidities, should be monitored for signs and symptoms of toxicity, overdose or withdrawal caused by increased or decreased levels of buprenorphine. Buprenorphine should be used with care in patients with respiratory insufficiency. Buprenorphine may cause drowsiness particularly when taken together with alcohol or central nervous system depressants such as benzodiazepines, tranquilisers, sedatives, gabapentinoids or hypnotics. Buprenorphine is a partial agonist at the mu-opiate receptor and chronic administration can produce opioid dependence. Serotonergic medicinal products, such as MAO inhibitors, selective serotonin re-uptake inhibitors (SSRIs), serotonin norepinephrine re-uptake inhibitors (SNRIs) or tricyclic antidepressants as the risk of serotonin syndrome, a potentially life-threatening condition, is increased. Baseline liver function tests and documentation of viral hepatitis status are recommended prior to starting therapy. Buprenorphine products have caused precipitated withdrawal symptoms in opioid-dependent patients when administered before the agonist effects resulting from recent opioid use or misuse have subsided. Buprenorphine should be used with caution in patients with moderate hepatic impairment. Hepatic function should be monitored regularly whilst on treatment. The use of buprenorphine is contraindicated in patients with severe hepatic impairment. Caution is recommended when dosing patients with severe renal impairment. Caution should be exercised when co-administering Buvidal® with other medicinal products that prolong the QT interval and in patients with a history of long QT syndrome or other risk factors for QT prolongation. For management of acute pain during continued use of Buvidal®, a combination of use of opioids with high mu-opioid receptor affinity (e.g. fentanyl), non-opioid analgesics and regional anaesthesia might be necessary. Titration of oral or intravenous short-acting opioid pain medicinal products (immediate-release morphine, oxycodone or fentanyl) to the desired analgesic effect in patients treated with Buvidal® might require higher doses. Patients should be monitored during treatment. Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the total opioid dosage. *Interactions:* No interaction studies have been performed with Buvidal®. See SmPC for precautions when co-administering buprenorphine with other drugs. *Fertility, pregnancy and lactation:* Buprenorphine should be used during pregnancy only if the potential benefit outweighs the potential risk to the foetus. Towards the end of pregnancy, buprenorphine may induce respiratory depression in the newborn infant even after a short period of administration. Buprenorphine and its metabolites are excreted in human breast milk and Buvidal® should be used with caution during breast-feeding. There are no or limited data on effects of buprenorphine on human fertility. *Driving and operating machines:* Buprenorphine has minor to moderate influence on the ability to drive and use machines when administered to opioid-dependent patients. The patient should be cautioned not to drive or operate hazardous machinery whilst taking this medicine until it is known how the patient is affected by the medicine. **Undesirable effects:** The adverse reactions most frequently reported for buprenorphine are headache, nausea, hyperhidrosis, insomnia, drug withdrawal syndrome and pain. *Very common (≥1/10):* insomnia, headache, nausea, hyperhidrosis, drug withdrawal syndrome, pain. *Injection site reactions:* in the double-blind, phase 3 efficacy trial, injection site-related adverse reactions were observed in 36 (16.9%) of the 213 patients (5% of the administered injections) in the Buvidal® treatment group. The most common adverse reactions were injection site pain (8.9%), injection site pruritus (6.1%) and injection site erythema (4.7%). The injection site reactions were all mild or moderate in severity and most events were transient. See full SmPC for further details of adverse reactions. **Overdose:** General supportive measures should be instituted, including close monitoring of respiratory and cardiac status of the patient. Symptomatic treatment of respiratory depression, following standard intensive care measures, should be instituted. The long duration of action of buprenorphine and the prolonged release from Buvidal®, should be taken into consideration when determining length of treatment needed to reverse the effects of an overdose. **Package quantities:** Pack contains 1 pre-filled syringe with stopper, needle, needle shield, safety device and 1 plunger rod. Pre-filled syringes for weekly injection: 8 mg, 16 mg, 24 mg, 32 mg. Pre-filled syringes for monthly injection: 64 mg, 96 mg, 128 mg, 160 mg. **Marketing authorisation numbers:** EU/1/18/1336/001, EU/1/18/1336/002, EU/1/18/1336/003, EU/1/18/1336/004, EU/1/18/1336/005, EU/1/18/1336/006, EU/1/18/1336/007 EU/1/18/1336/009. **Legal category:** Prescription medicine. Further information is available from the **Marketing Authorisation Holder:** Camurus AB, Ideon Science Park, SE-223 70 Lund, Sweden. Phone: +800 2577 2577. The text is based on the SmPC: May 2021. *Internal approval: INT-BUV-2100012.*

Adverse events should be reported according to national guidelines.


Thank you!
Questions welcome!

Treatment Satisfaction Questionnaire for Medication (TSQM)

- TSQM (version 1.4): a validated PRO instrument developed in 2004.[1] It has been studied in many chronic diseases including in patients with opioid dependence treated with methadone[2,3] and buprenorphine.[4]
- 14 questions with responses obtained on a 5- or 7-point Likert scale, and yes/no response for side-effects.[1]
- The questions are in four domains/subscales:[1]
  - Global Satisfaction (3 questions)
  - Convenience (3 questions)
  - Effectiveness (3 questions)
  - Side Effects (5 questions)
- The subscale scores are transformed into TSQM scores ranging from 0–100.[1]
- A TSQM global satisfaction score of ≥ 80 has been used as a cut-off point for satisfaction with medication in other diseases such as rheumatoid arthritis.[5]

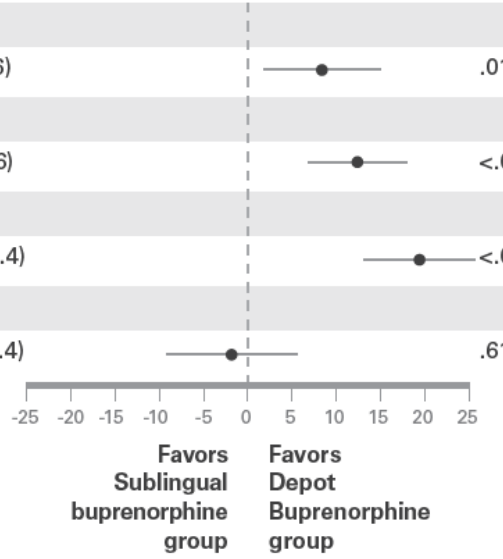
PRO, patient reported outcome

Source: 1. Atkinson MJ, et al. Health Qual Life Outcomes. 2004;2:12. 2. Trujols J, et al. J Clin Psychopharmacol. 2012;32:69–74. 3. de los Cobos JP, et al. Drug Alcohol Depend. 2014;142:79–85. 4. de los Cobos JP, et al. Int J Drug Policy 2018;58:126–134. 5. Radawski C, et al. Rheumatol Ther. 2019; 6: 461–471.

Buvidal TSQM effectiveness and convenience scores were significantly higher

at Week 24 ($p<0.001$), with no difference in safety domain scores vs. SL BPN/NX ($p=0.61$)

Variable	Mean score (SE): Depot Buprenorphine (n=60)	Mean score (SE): Sublingual buprenorphine (n=59)	Treatment difference based on normalized score (95% CI), %	P value
TSQM global satisfaction				
Week 24	82.5 (2.3)	74.3 (2.3)	8.2 (1.7 to 14.6)	.01
TSQM effectiveness				
Week 24	87.2 (1.9)	75.0 (1.9)	12.2 (6.8 to 17.6)	<.001
TSQM convenience				
Week 24	88.7 (2.2)	69.6 (2.2)	19.1 (12.9 to 25.4)	<.001
TSQM side effects				
Week 24	88.5 (2.6)	90.3 (2.6)	–1.8 (–9.0 to 5.4)	.61

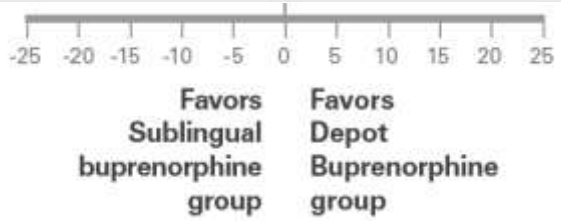


SL BPN/NX: sublingual buprenorphine/naloxone; TSQM: Treatment Satisfaction Questionnaire for Medication.

Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

Buvidal improved PROs vs. SL BPN/NX

Variable	Mean score (SE): Depot Buprenorphine (n=60)	Mean score (SE): Sublingual buprenorphine (n=59)	Treatment difference based on normalized score (95% CI), %	P value
PS-VAS				
Week 24	85.4 (2.4)	78.8 (2.4)	6.6 (–0.1 to 13.3)	.05
PGI-I score				
Week 24	2.0 (0.2)	2.9 (0.2)	13.0 (6.9 to 19.1)	<.001
TBQ global score				
Week 24	13.3 (2.6)	28.6 (2.5)	10.3 (5.5 to 15.0)	<.001
ORBIT total score				
Week 24	0.5 (0.2)	1.2 (0.2)	1.8 (0.5 to 3.0)	.006
SURE total score				
Week 24	52.8 (1.0)	54.7 (1.0)	–3.0 (–7.4 to 1.5)	.19
SF-36 physical component summary measure				
Week 24	50.7 (0.9)	48.0 (0.9)	2.7 (0.1 to 5.3)	.04
SF-36 mental component summary measure				
Week 24	43.7 (1.4)	41.7 (1.4)	2.0 (–1.8 to 5.9)	.30

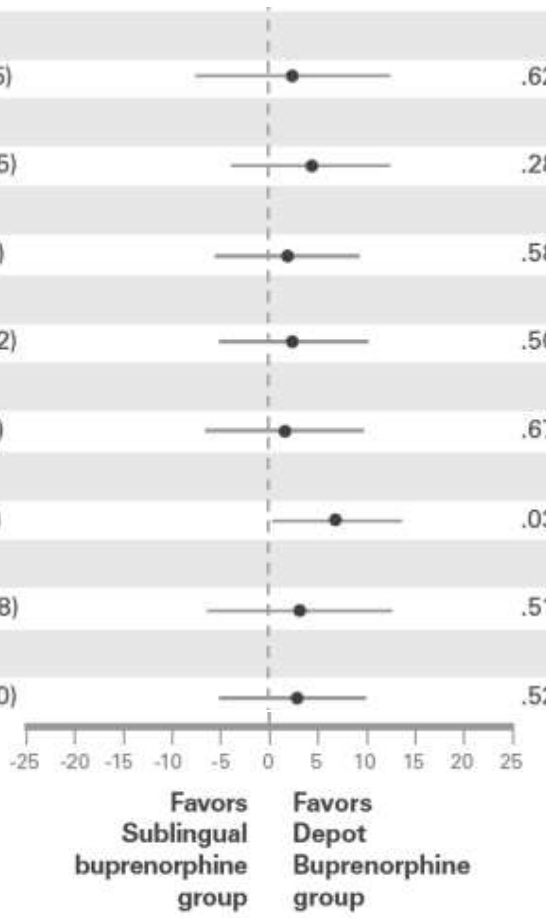


PRO, patient reported outcome; SL BPN/NX, sublingual buprenorphine/naloxone.

Source: Lintzeris N et al. JAMA Netw Open. 2021;4(5):e219041.

Buvidal improved PROs vs. SL BPN/NX

Variable	Mean score (SE): Depot Buprenorphine (n=60)	Mean score (SE): Sublingual buprenorphine (n=59)	Treatment difference based on normalized score (95% CI), %	P value
OSTQoL overall quality of life				
Week 24	2.6 (0.1)	2.5 (0.1)	2.5 (–7.5 to 12.5)	.62
OSTQoL personal development				
Week 24	2.4 (0.1)	2.2 (0.1)	4.5 (–3.8 to 12.5)	.28
OSTQoL mental distress				
Week 24	2.5 (0.1)	2.4 (0.1)	2.0 (–5.2 to 9.5)	.58
OSTQoL social contacts				
Week 24	2.7 (0.1)	2.6 (0.1)	2.5 (–5.0 to 10.2)	.50
OSTQoL material well-being				
Week 24	2.8 (0.1)	2.7 (0.1)	1.8 (–6.5 to 9.8)	.67
OSTQoL opioid substitution treatment				
Week 24	3.3 (0.1)	3.0 (0.1)	7.0 (0.5 to 13.8)	.03
OSTQoL discrimination				
Week 24	2.5 (0.1)	2.4 (0.1)	3.2 (–6.2 to 12.8)	.51
EQ-5D-3L, index value				
Week 24	0.7 (0.0)	0.7 (0.0)	3.0 (–5.0 to 10.0)	.52



PRO, patient reported outcome; SL BPN/NX, sublingual buprenorphine/naloxone.

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