



Clinical trial results:

An Open-Label Multicenter Study Assessing the Long-Term Safety of a Once-Weekly and Once-Monthly, Long-Acting Subcutaneous Injection Depot of Buprenorphine (CAM2038) in Adult Outpatients with Opioid Use Disorder

Summary

EudraCT number	2015-003035-35
Trial protocol	GB SE DK HU
Global end of trial date	12 April 2017

Results information

Result version number	v1 (current)
This version publication date	11 May 2019
First version publication date	11 May 2019

Trial information

Trial identification

Sponsor protocol code	HS-14-499
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02672111
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Braeburn Inc.
Sponsor organisation address	450 Plymouth Rd., Suite 400, Plymouth Meeting, PA, United States, 19462
Public contact	Sonnie Kim, PharmD, Braeburn Inc. , 609 751-5375,
Scientific contact	Sonnie Kim, PharmD, Braeburn Inc. , 609 751-5375,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 April 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to demonstrate the safety and tolerability of CAM2038 products in 12-month (48-week) Buprenorphine (BPN) treatment in adult outpatients with opioid use disorder.

Protection of trial subjects:

Before the study was initiated, the protocol was submitted to the Institutional Review Boards/Independent Ethics Committees (IRBs/IECs) according to national or local regulations. Protocol amendments issued during the study were also submitted. The Investigator conducted the study in accordance with GCP and all applicable regulations, including, where applicable, the Declaration of Helsinki. The Investigator (or authorized designee) ensured that the subject (or the subject's legal representative) was given full and adequate oral and written information about the nature, purpose, potential and possible risks and benefits of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Denmark: 20
Country: Number of subjects enrolled	Germany: 34
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Australia: 25
Country: Number of subjects enrolled	United States: 127
Worldwide total number of subjects	228
EEA total number of subjects	76

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	226
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This multicenter trial was conducted at 29 sites (with 28 investigators) in the United States, United Kingdom, Hungary, Denmark, Sweden, Germany, and Australia; of these, 26 sites enrolled subjects.

Pre-assignment

Screening details:

Screening Phase started within 1-3 weeks of Day 1 of the Treatment Phase. All assessments were conducted at Screening as per the Schedule of Procedures and Assessments. All subjects underwent screening procedures.

Period 1

Period 1 title	Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Receiving Sublingual BPN (SL BPN) at Entry

Arm description:

Subjects who were receiving SL BPN or SL BPN/naloxone (SL BPN/NX) at entry transitioned to CAM2038 once weekly (q1w) or once monthly (q4w) subcutaneous (SC) injections according to their current dose of SL BPN or SL BPN/NX. Subjects were advised not to take their ordinary SL BPN (or BPN/NX) tablet(s) on Day 1 (i.e., the last dose of SL BPN [or BPN/NX] was taken on the day before dosing with CAM2038 q1w or CAM2038 q4w). During the 48-week treatment period, subjects could switch between doses of CAM2038 and between treatment with CAM2038 q1w and CAM2038 q4w.

Arm type	Experimental
Investigational medicinal product name	CAM2038 q1w
Investigational medicinal product code	
Other name	BPN FluidCrystal® Injection depot for once weekly administration
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

CAM2038 administered, 50 mg/mL: 8, 16, 24, and 32 mg (BPN base), 0.16, 0.32, 0.48, and 0.64 mL SC injection

Investigational medicinal product name	CAM2038 q4w
Investigational medicinal product code	
Other name	BPN FluidCrystal® Injection depot for once monthly administration
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

CAM2038 administered, 356 mg/mL: 64, 96, 128, and 160 mg (BPN base), 0.18, 0.27, 0.36, and 0.45 mL SC injection

Arm title	New to BPN Treatment
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Arm description:

For subjects who were not receiving SL BPN or SL BPN/NX at entry, treatment was initiated with a single CAM2038 q1w 16 mg SC injection (following a 4 mg SL BPN/NX test dose); additional dose adjustments were allowed up to maximum weekly dose of 40 mg (the maximum weekly dose was increased from 32 to 40 mg). During the 48-week treatment period, subjects could switch between doses of CAM2038 and between treatment with CAM2038 q1w and CAM2038 q4w.

Arm type	Experimental
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Investigational medicinal product name	CAM2038 q1w
Investigational medicinal product code	
Other name	BPN FluidCrystal® Injection depot for once weekly administration
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

CAM2038 administered, 16 mg SC injection, additional dose adjustments were allowed up to maximum weekly dose of 40 mg (the maximum weekly dose was increased from 32 to 40 mg)

Investigational medicinal product name	CAM2038 q4w
Investigational medicinal product code	
Other name	BPN FluidCrystal® Injection depot for once monthly administration
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

CAM2038 administered, 356 mg/mL: 64, 96, 128, and 160 mg (BPN base), 0.18, 0.27, 0.36, and 0.45 mL SC injection

Investigational medicinal product name	SL BPN/NX
Investigational medicinal product code	
Other name	Suboxone®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects who were not receiving SL BPN or SL BPN/NX at entry received a 4 mg test dose of SL BPN/NX on Day 1 to assess tolerability. The SL BPN/NX test dose consisted of 2 SL tablets of Suboxone®, each containing 2 mg BPN and 0.5 mg naloxone.

Number of subjects in period 1^[1]	Receiving Sublingual BPN (SL BPN) at Entry	New to BPN Treatment
Started	190	37
Completed	132	25
Not completed	58	12
Physician decision	5	-
Consent withdrawn by subject	31	2
Adverse event, non-fatal	3	1
Other	2	-
Pregnancy	1	-
Lost to follow-up	4	9
Lack of efficacy	12	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Overall, 265 subjects were screened for the study, and 228 subjects were enrolled. One subject withdrew consent prior to receiving the first dose of CAM2038, and 227 subjects received at least one dose of CAM2038

Baseline characteristics

Reporting groups

Reporting group title	Receiving Sublingual BPN (SL BPN) at Entry
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Reporting group description:

Subjects who were receiving SL BPN or SL BPN/naloxone (SL BPN/NX) at entry transitioned to CAM2038 once weekly (q1w) or once monthly (q4w) subcutaneous (SC) injections according to their current dose of SL BPN or SL BPN/NX. Subjects were advised not to take their ordinary SL BPN (or BPN/NX) tablet(s) on Day 1 (i.e., the last dose of SL BPN [or BPN/NX] was taken on the day before dosing with CAM2038 q1w or CAM2038 q4w). During the 48-week treatment period, subjects could switch between doses of CAM2038 and between treatment with CAM2038 q1w and CAM2038 q4w.

Reporting group title	New to BPN Treatment
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Reporting group description:

For subjects who were not receiving SL BPN or SL BPN/NX at entry, treatment was initiated with a single CAM2038 q1w 16 mg SC injection (following a 4 mg SL BPN/NX test dose); additional dose adjustments were allowed up to maximum weekly dose of 40 mg (the maximum weekly dose was increased from 32 to 40 mg). During the 48-week treatment period, subjects could switch between doses of CAM2038 and between treatment with CAM2038 q1w and CAM2038 q4w.

Reporting group values	Receiving Sublingual BPN (SL BPN) at Entry	New to BPN Treatment	Total
Number of subjects	190	37	227
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	41.3	41.8	
standard deviation	± 9.64	± 9.41	-
Gender categorical Units: Subjects			
Female	71	13	84
Male	119	24	143

End points

End points reporting groups

Reporting group title	Receiving Sublingual BPN (SL BPN) at Entry
Reporting group description:	
Subjects who were receiving SL BPN or SL BPN/naloxone (SL BPN/NX) at entry transitioned to CAM2038 once weekly (q1w) or once monthly (q4w) subcutaneous (SC) injections according to their current dose of SL BPN or SL BPN/NX. Subjects were advised not to take their ordinary SL BPN (or BPN/NX) tablet(s) on Day 1 (i.e., the last dose of SL BPN [or BPN/NX] was taken on the day before dosing with CAM2038 q1w or CAM2038 q4w). During the 48-week treatment period, subjects could switch between doses of CAM2038 and between treatment with CAM2038 q1w and CAM2038 q4w.	
Reporting group title	New to BPN Treatment
Reporting group description:	
For subjects who were not receiving SL BPN or SL BPN/NX at entry, treatment was initiated with a single CAM2038 q1w 16 mg SC injection (following a 4 mg SL BPN/NX test dose); additional dose adjustments were allowed up to maximum weekly dose of 40 mg (the maximum weekly dose was increased from 32 to 40 mg). During the 48-week treatment period, subjects could switch between doses of CAM2038 and between treatment with CAM2038 q1w and CAM2038 q4w.	

Primary: Number of subjects with Adverse events (AEs)

End point title	Number of subjects with Adverse events (AEs) ^[1]
End point description:	
An AE is any untoward medical occurrence in a subject administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (e.g., including an abnormal laboratory finding), symptom, or increase in severity of a preexisting abnormality, temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product. Treatment-emergent adverse event (TEAE) have been presented in the table below.	
End point type	Primary
End point timeframe:	
Adverse events were collected from the time of informed consent until 14 days after the Follow-up Visit (or 30 days after early termination)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis is available for primary endpoint.

End point values	Receiving Sublingual BPN (SL BPN) at Entry	New to BPN Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	37		
Units: Subjects				
number (not applicable)				
Subject had at least 1 TEAE	131	12		
Subject had at least 1 drug-related TEAE	58	2		
Subject had at least 1 severe TEAE	13	2		
Deaths	0	0		
Subject had at least 1 non-fatal serious AE (SAE)	10	2		
Subject had at least 1 non-fatal, drug-related SAE	0	0		
Hospitalizations	9	1		

Subject discontinued study drug due to a TEAE	4	1		
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Statistical analyses

No statistical analyses for this end point

Secondary: Mean Percentage of Negative Urine Toxicology Results for Illicit Opioid Use Supported by Self-Reported Illicit Opioid Use

End point title	Mean Percentage of Negative Urine Toxicology Results for Illicit Opioid Use Supported by Self-Reported Illicit Opioid Use
End point description: Evaluate efficacy of CAM2038 through efficacy parameters such as urine toxicology results for illicit opioids.	
End point type	Secondary
End point timeframe: 12 months (48 weeks)	

End point values	Receiving Sublingual BPN (SL BPN) at Entry	New to BPN Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	37		
Units: Percentage				
arithmetic mean (standard deviation)				
Negative Urine Toxicology Results (n = 189, 37)	82.8 (± 29.31)	41.2 (± 34.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Retention in treatment over time

End point title	Retention in treatment over time
End point description: Evaluate efficacy of CAM2038 through efficacy parameters such as retention in treatment over time.	
End point type	Secondary
End point timeframe: 12 months (48 weeks)	

End point values	Receiving Sublingual BPN (SL BPN) at Entry	New to BPN Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	37		
Units: Weeks				
arithmetic mean (standard deviation)	38.3 (± 16.85)	43.6 (± 11.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Measures of opioid withdrawal: Clinical Opiate Withdrawal Scale (COWS)

End point title	Measures of opioid withdrawal: Clinical Opiate Withdrawal Scale (COWS)
End point description: Evaluate efficacy of CAM2038 through efficacy parameters such as measures of withdrawal (COWS). Study personnel assessed clinical observations indicative of withdrawal using the COWS. This scale consists of 11 common opiate withdrawal signs or symptoms, rated on a numeric scale from 0 to 4 or 5 and based on a timed period of observation of the subject by the rater. Higher scores are associated with greater withdrawal symptoms with a total range for all items of between 0-48.	
End point type	Secondary
End point timeframe: 12 months (48 weeks)	

End point values	Receiving Sublingual BPN (SL BPN) at Entry	New to BPN Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	37		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (n = 190, 37)	2.0 (± 2.7)	10.6 (± 3.7)		
Visit 3 Day 8 (n = 103, 36)	3.7 (± 4.1)	3.0 (± 2.5)		
Visit 26 Day 169 (n = 114, 26)	1.9 (± 2.8)	0.2 (± 0.4)		
EOT Day 337 (n = 138, 29)	1.4 (± 2.3)	0.3 (± 0.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Measures of opioid withdrawal: Subjective Opiate Withdrawal Scale (SOWS)

End point title	Measures of opioid withdrawal: Subjective Opiate Withdrawal Scale (SOWS)
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End point description:

Evaluate efficacy of CAM2038 through efficacy parameters such as measures of withdrawal (SOWS). Subjects completed a self-assessment of withdrawal symptoms using the SOWS. This form contains 16 questions that rate the intensity of withdrawal from 0 ("Not at all") to 4 ("Extremely"), with higher scores associated with greater withdrawal symptoms and total range for all items of 0-64.

End point type Secondary

End point timeframe:

12 months (48 weeks)

End point values	Receiving Sublingual BPN (SL BPN) at Entry	New to BPN Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	37		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (n = 190, 37)	4.7 (± 8.1)	27.1 (± 15.3)		
Visit 3 Day 8 (n = 103, 36)	8.4 (± 11.5)	8.9 (± 10.9)		
Visit 26 Day 169 (n = 114, 26)	4.3 (± 7.2)	3.0 (± 7.5)		
EOT Day 337 (n = 138, 29)	3.3 (± 6.3)	3.9 (± 8.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Measures of opioid craving (Desire to Use Visual analog scale [VAS])

End point title Measures of opioid craving (Desire to Use Visual analog scale [VAS])

End point description:

Evaluate efficacy of CAM2038 through efficacy parameters such as measures of craving (desire to use VAS). Desire to Use assessments were performed using a unipolar 100 mm VAS. Subjects were asked "Since your last scheduled assessment visit, indicate your worst or strongest desire to use opioids, where 0 = No desire to use and 100 mm = Strongest possible desire".

End point type Secondary

End point timeframe:

12 months (48 weeks)

End point values	Receiving Sublingual BPN (SL BPN) at Entry	New to BPN Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	37		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (n = 189, 37)	11.7 (± 24.2)	74.8 (± 24.8)		

Visit 3 Day 8 (n = 103, 36)	18.8 (± 29.8)	23.0 (± 25.9)		
Visit 26 Day 169 (n = 113, 26)	6.4 (± 15.6)	5.8 (± 16.7)		
EOT Day 337 (n = 138, 28)	6.4 (± 16.5)	2.8 (± 6.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Measures of opioid craving (Need to Use VAS)

End point title	Measures of opioid craving (Need to Use VAS)
End point description: Evaluate efficacy of CAM2038 through efficacy parameters such as measures of craving (need to use VAS). Need to use assessments were performed using a unipolar 100 mm VAS. Subjects were asked "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".	
End point type	Secondary
End point timeframe: 12 months (48 weeks)	

End point values	Receiving Sublingual BPN (SL BPN) at Entry	New to BPN Treatment		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	37		
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Baseline (n = 190, 37)	11.7 (± 23.8)	76.3 (± 24.9)		
Visit 3 Day 8 (n = 103, 36)	18.0 (± 27.9)	34.3 (± 29.2)		
Visit 26 Day 169 (n = 114, 26)	5.6 (± 12.5)	8.0 (± 18.2)		
EOT Day 337 (n = 138, 28)	5.4 (± 14.3)	5.3 (± 15.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from the time of informed consent until 14 days after the Follow-up Visit (or 30 days after early termination)

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Receiving Sublingual (SL) BPN (SL BPN) at Entry
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Reporting group description:

Subjects who were receiving SL BPN or SL BPN/naloxone (SL BPN/NX) at entry transitioned to CAM2038 once weekly (q1w) or once monthly (q4w) subcutaneous (SC) injections according to their current dose of SL BPN or SL BPN/NX. Subjects were advised not to take their ordinary SL BPN (or BPN/NX) tablet(s) on Day 1 (i.e., the last dose of SL BPN [or BPN/NX] was taken on the day before dosing with CAM2038 q1w or CAM2038 q4w). During the 48-week treatment period, subjects could switch between doses of CAM2038 and between treatment with CAM2038 q1w and CAM2038 q4w.

Reporting group title	New to BPN Treatment
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Reporting group description:

For subjects who were not receiving SL BPN or SL BPN/NX at entry, treatment was initiated with a single CAM2038 q1w 16 mg SC injection (following a 4 mg SL BPN/NX test dose); additional dose adjustments were allowed up to maximum weekly dose of 40 mg (the maximum weekly dose was increased from 32 to 40 mg). During the 48-week treatment period, subjects could switch between doses of CAM2038 and between treatment with CAM2038 q1w and CAM2038 q4w.

Serious adverse events	Receiving Sublingual (SL) BPN (SL BPN) at Entry	New to BPN Treatment	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 190 (5.26%)	2 / 37 (5.41%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Follicular thyroid cancer			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Multiple injuries			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Ventricular tachycardia			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 190 (0.53%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Drug withdrawal syndrome			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Duodenitis			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychotic disorder			

subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Substance-induced psychotic disorder			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc degeneration			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 190 (0.53%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 190 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Receiving Sublingual (SL) BPN (SL BPN) at Entry	New to BPN Treatment	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	130 / 190 (68.42%)	12 / 37 (32.43%)	
Nervous system disorders			
Headache			
subjects affected / exposed	18 / 190 (9.47%)	0 / 37 (0.00%)	
occurrences (all)	23	0	
General disorders and administration site conditions			

Injection site pain subjects affected / exposed occurrences (all)	33 / 190 (17.37%) 67	2 / 37 (5.41%) 7	
Injection site swelling subjects affected / exposed occurrences (all)	25 / 190 (13.16%) 37	2 / 37 (5.41%) 8	
Injection site erythema subjects affected / exposed occurrences (all)	20 / 190 (10.53%) 42	1 / 37 (2.70%) 1	
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	16 / 190 (8.42%) 17	0 / 37 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	12 / 190 (6.32%) 13	0 / 37 (0.00%) 0	
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	17 / 190 (8.95%) 28	1 / 37 (2.70%) 1	
Urinary tract infection subjects affected / exposed occurrences (all)	9 / 190 (4.74%) 11	3 / 37 (8.11%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 December 2015	Notable changes made to the protocol with Amendment 1: Added the US IND number. Added a time window (i.e., at least 60 days) for prior use of BPN at screening to better select subjects who are new entrants to the treatment. Corrected the number of subjects exposed to CAM2038 q1w and CAM2038 q4w based on final data from Study HS-13-487. Corrected the transition doses and clarified that subjects should not take their ordinary SL BPN or SL BPN/NX dose before dosing with CAM2038 q4w on Day 1. Clarified that substance abuse disorder included alcohol; added a criterion to exclude subjects with history or evidence of suicidal ideation or suicidal behavior. Added safety reasons for discontinuing a subject from the study and clarified that pregnant subjects had to be discontinued from the study in the United Kingdom. Clarified that substance abuse and treatment history would be obtained using questionnaires instead of an interview. Added alcohol to the panel of drugs analyzed in the urine samples. Removed the pharmacokinetic population as an analysis population.
12 July 2016	Notable changes made to the protocol with Amendment 2: Increased the sample size and dropout rate for the study with the addition of United States sites. Added efficacy measures to assess the subject quality of life while on study and subject satisfaction. Added/clarified text allowing for an additional SC supplemental injection of 8 mg CAM2038 q1w on top of the weekly dose of 32 mg, for a maximum weekly dose of 40 mg per week for subjects receiving CAM2038 q1w. Added/clarified text allowing for an additional SC booster injection of 8 mg CAM2038 q1w at a maximum of two supplemental injections per week for subjects receiving CAM2038 q4w.
18 November 2016	Notable changes made to the protocol with Amendment 3: Clarified that once all injections sites had been utilized and there were no additional new injection sites, a CAM2038 q4w injection could be injected into a previously used CAM2038 q1w injection site following the q1w rule (i.e., injection into the same site was only to occur after 8 weeks).
09 December 2016	Notable changes made to the protocol with Amendment 4: Added text describing the injection site examination to say that if needed, a photograph of the adverse site reactions would be taken and shared with the medical monitor for review. Further, the pain scale would be completed by the subjects within 10 minutes after each injection. Clarified the timeframes of monthly psychosocial counseling to say at least once every 4 weeks.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported