Clinical trial results:
A Multicentre, Single-Arm, Open-Label Study of the Repeated Administration of Qutenza^TM (Capsaicin (8%) high-concentration patch) for the Treatment of Peripheral Neuropathic Pain (PNP)

Summary

EudraCT number	2009-016457-18
Trial protocol	IE FR BE GB CZ FI ES AT IT HU NL SK PL SI GR
Global end of trial date	26 September 2013

Results information

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	23 May 2015
Version creation reason	• Correction of full data set Updates required due to non-substantial reasons

Trial information

Trial identification

Sponsor protocol code	E05-CL-3001/STRIDE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01252160
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Europe Ltd
Sponsor organisation address	2000 Hillswood Drive, Chertsey, United Kingdom, KT16 0RS
Public contact	Associate Medical Director - Pain Therapeutic Area, Astellas Pharma Europe Ltd, Astellas.resultsdisclosure@astellas.com
Scientific contact	Associate Medical Director - Pain Therapeutic Area, Astellas Pharma Europe Ltd, Astellas.resultsdisclosure@astellas.com

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	26 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 September 2013
Global end of trial reached?	Yes
Global end of trial date	26 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to assess the safety and efficacy of repeat applications of Qutenza TM (Capsaicin (8%) high-concentration patch) over 52 weeks in participants with Peripheral Neuropathic Pain (PNP).

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, ICH GCP Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki.Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information. Approval for the study protocol, dated 30 Apr 2010, was obtained from the relevant competent authorities prior to study initiation.

Background therapy:

Participants receiving first patch application could receive oral and transdermal opioid medication if it did not exceed a total oral daily dose of morphine of 80 mg or the equivalent, which was to be calculated using the Opioid Equivalence Guidance. Any changes, additions or discontinuations to medications were assessed and recorded at every study visit. A short acting opioid could be administered to relieve treatment-associated discomfort during and/or after treatment procedures, while the patient was in the clinic. Participants could receive concomitant systemic non-opioid pain medications for the treatment of Peripheral Neuropathic Pain(PNP).

Evidence for comparator: -

Actual start date of recruitment	28 October 2010
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	Netherlands: 11
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Romania: 12
Country: Number of subjects enrolled	Slovakia: 5
Country: Number of subjects enrolled	Slovenia: 3
Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	United Kingdom: 73
Country: Number of subjects enrolled	Austria: 15
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	Czech Republic: 16

Country: Number of subjects enrolled	Finland: 13
Country: Number of subjects enrolled	France: 40
Country: Number of subjects enrolled	Greece: 9
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Ireland: 7
Country: Number of subjects enrolled	Italy: 34
Worldwide total number of subjects	306
EEA total number of subjects	306

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)	197
From 65 to 84 years	102
85 years and over	7

Subject disposition

Recruitment

Recruitment details:

This open-label, single-arm, multicenter study was conducted at 63 sites in Europe: 3 in Austria, 5 in Belgium, 4 in Czech Republic, 2 in Finland, 6 in France,2 in Greece, 1 in Hungary, 2 in Ireland, 9 in Italy, 2 in Netherlands, 3 in Poland, 2 in Romania, 1 in Slovakia, 2 in Slovenia, 10 in Spain, and 9 in the UK.

Pre-assignment

Screening details:

Study population consisted of 306 enrolled non-diabetic adult participants (18-90 years) with moderate to severe pain due to Peripheral Neuropathic Pain (PNP) with Postherpetic Neuralgia (PHN), HIV-associated Neuropathy (HIV-AN), Post-traumatic Nerve Injury (PNI) and Idiopatic Small Nerve Neuropathy (ISNN).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	PHN [Post-herpetic Neuralgia]

Arm description:

Participants with identified postherpetic neuralgia.

Arm type	Experimental
Investigational medicinal product name	Qutenza [Capsaicin (8%) high-concentration patch]
Investigational medicinal product code	ASP0805
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Topical use

Dosage and administration details:

Qutenza is a high-concentration (8%) capsaicin patch which was applied to intact, non-irritated, dry skin. Each patch contained a total of 179 mg of capsaicin or 640 µg of capsaicin per cm2 of patch (8%). Up to 4 patches (1120 cm2) could be applied at any 1 application.The patches were applied for 30 min (feet) or 60 min (other body locations). Patients were pre-treated with a local topical anesthetic (for a period as determined by the prescribing information of the product used) prior to the patch application. The choice of topical anesthetic was at the investigator’s discretion. After topical anesthetic was removed Qutenza was applied to painful area(s). Following removal of the patch treated area was cleaned with the gel provided.

Arm title	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]

Arm description:

Participants with identified human immunodeficiency virus-associated neuropathy.

Arm type	Experimental
Investigational medicinal product name	Qutenza [Capsaicin (8%) high-concentration patch]
Investigational medicinal product code	ASP0805
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Topical use

Dosage and administration details:

Qutenza is a high-concentration (8%) capsaicin patch which was applied to intact, non-irritated, dry skin. Each patch contained a total of 179 mg of capsaicin or 640 µg of capsaicin per cm^2 of patch (8%). Up to 4 patches (1120 cm2) could be applied at any 1 application.The patches were applied for 30 min (feet) or 60 min (other body locations). Patients were pre-treated with a local topical anesthetic (for a period as determined by the prescribing information of the product used) prior to the patch

application. The choice of topical anesthetic was at the investigator's discretion. After topical anesthetic was removed Qutenza was applied to painful area(s). Following removal of the patch treated area was cleaned with the gel provided.

Arm title	PNI [Post-traumatic Nerve Injury]

Arm description:

Participants with identified post-traumatic nerve injury.

Arm type	Experimental
Investigational medicinal product name	Qutenza [Capsaicin (8%) high-concentration patch]
Investigational medicinal product code	ASP0805
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Topical use

Dosage and administration details:

Qutenza is a high-concentration (8%) capsaicin patch which was applied to intact, non-irritated, dry skin. Each patch contained a total of 179 mg of capsaicin or 640 µg of capsaicin per cm^2 of patch (8%). Up to 4 patches (1120 cm^2) could be applied at any 1 application.The patches were applied for 30 min(feet) or 60 min (other body locations). Patients were pre-treated with a local topical anesthetic (for a period as determined by the prescribing information of the product used) prior to the patch application. The choice of topical anesthetic was at the investigator's discretion. After topical anesthetic was removed Qutenza was applied to painful area(s). Following removal of the patch treated area was cleaned with the gel provided.

Arm title	Other type of Peripheral Neuropathic Pain [PNP]

Arm description:

Participants with identified peripheral neuropathic pain.

Arm type	Experimental
Investigational medicinal product name	Qutenza [Capsaicin (8%) high-concentration patch]
Investigational medicinal product code	ASP0805
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Topical use

Dosage and administration details:

Qutenza is a high-concentration (8%) capsaicin patch which was applied to intact, non-irritated, dry skin. Each patch contained a total of 179 mg of capsaicin or 640 µg of capsaicin per cm^2 of patch (8%). Up to 4 patches (1120 cm^2) could be applied at any 1 application.The patches were applied for 30 min (feet) or 60 min (other body locations). Patients were pre-treated with a local topical anesthetic (for a period as determined by the prescribing information of the product used) prior to the patch application. The choice of topical anesthetic was at the investigator's discretion. After topical anesthetic was removed Qutenza was applied to painful area(s). Following removal of the patch treated area was cleaned with the gel provided.

Number of subjects in period 1	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]
Started	107	80	99
Completed	66	45	54
Not completed	41	35	45
Consent withdrawn by subject	11	13	8
Adverse Event	5	1	4

Other	1	5	2
Protocol Violation	3	2	1
Lost to follow-up	5	6	6
Lack of efficacy	16	8	24

Number of subjects in period 1	Other type of Peripheral Neuropathic Pain [PNP]
Started	20
Completed	11
Not completed	9
Consent withdrawn by subject	1
Adverse Event	1
Other	1
Protocol Violation	-
Lost to follow-up	-
Lack of efficacy	6

Baseline characteristics

Reporting groups	
Reporting group title	PHN [Post-herpetic Neuralgia]
Reporting group description:	
Participants with identified postherpetic neuralgia.	
Reporting group title	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]
Reporting group description:	
Participants with identified human immunodeficiency virus-associated neuropathy.	
Reporting group title	PNI [Post-traumatic Nerve Injury]
Reporting group description:	
Participants with identified post-traumatic nerve injury.	
Reporting group title	Other type of Peripheral Neuropathic Pain [PNP]
Reporting group description:	
Participants with identified peripheral neuropathic pain.	

Reporting group values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]
Number of subjects	107	80	99
Age categorical			
The mean age of patients enrolled in the study was 57.9 years in the range from 20 to 90 years. The oldest patients were in the Postherpetic neuralgia (PHN) group with mean age 70.5 years and the range from 36 to 90 years. The youngest patients were in the Human immunodeficiency virus-associated neuropathy (HIV-AN) group with mean age of 51.5 years and the range of 22 to 76 years. The Post traumatic nerve injury (PNI) group had a mean age of 49.7 years and the age range from 20 to 81 years.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	27	71	83
From 65-84 years	36	8	11
85 years and over	44	1	5
Age continuous			
Units: years			
arithmetic mean	70.5	51.5	49.7
standard deviation	± 10.85	± 10.97	± 13.48
Gender categorical			
Units: Subjects			
Female	50	15	55
Male	57	65	44
Brief Pain Inventory (BPI-DN Question 5) baseline average pain			
Brief Pain Inventory (BPI) questions are based on a scale of 1 (no pain) to 10 (pain as bad as can be imagined). BPI-DN Question 5 was used to assess participants baseline average pain.			

Units: Number			
arithmetic mean	6.2	6.1	6.6
standard deviation	± 1.55	± 1.75	± 1.68
Time Since Diagnosis of Neuropathic Pain (Years)			
Time since diagnosis is defined as the date of baseline visit minus the date when diagnosis was made plus 1 day divided by 365.25. Time since diagnosis is presented for all groups, Human immunodeficiency virus-associated neuropathy (HIV-AN; N=79), Postherpetic neuralgia (PHN; N=107) and Post-traumatic nerve injury (PNI; N=99).			
Units: Years			
arithmetic mean	3.9	7.4	4
standard deviation	± 4.97	± 5.78	± 4.34

Reporting group values	Other type of Peripheral Neuropathic Pain [PNP]	Total	
Number of subjects	20	306	
Age categorical			
The mean age of patients enrolled in the study was 57.9 years in the range from 20 to 90 years. The oldest patients were in the Postherpetic neuralgia (PHN) group with mean age 70.5 years and the range from 36 to 90 years. The youngest patients were in the Human immunodeficiency virus-associated neuropathy (HIV-AN) group with mean age of 51.5 years and the range of 22 to 76 years. The Post traumatic nerve injury (PNI) group had a mean age of 49.7 years and the age range from 20 to 81 years.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	16	197	
From 65-84 years	3	58	
85 years and over	1	51	
Age continuous			
Units: years			
arithmetic mean	56.5		
standard deviation	± 10.84	-	
Gender categorical			
Units: Subjects			
Female	12	132	
Male	8	174	
Brief Pain Inventory (BPI-DN Question 5) baseline average pain			
Brief Pain Inventory (BPI) questions are based on a scale of 1 (no pain) to 10 (pain as bad as can be imagined). BPI-DN Question 5 was used to assess participants baseline average pain.			
Units: Number			
arithmetic mean	6.4		
standard deviation	± 1.38	-	
Time Since Diagnosis of Neuropathic Pain (Years)			
Time since diagnosis is defined as the date of baseline visit minus the date when diagnosis was made plus 1 day divided by 365.25. Time since diagnosis is presented for all groups, Human immunodeficiency virus-associated neuropathy (HIV-AN; N=79), Postherpetic neuralgia (PHN; N=107) and Post-traumatic nerve injury (PNI; N=99).			

Units: Years			
arithmetic mean	7.7		
standard deviation	± 7.98	-	

End points

End points reporting groups

Reporting group title	PHN [Post-herpetic Neuralgia]
Reporting group description:	
Participants with identified postherpetic neuralgia.	
Reporting group title	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]
Reporting group description:	
Participants with identified human immunodeficiency virus-associated neuropathy.	
Reporting group title	PNI [Post-traumatic Nerve Injury]
Reporting group description:	
Participants with identified post-traumatic nerve injury.	
Reporting group title	Other type of Peripheral Neuropathic Pain [PNP]
Reporting group description:	
Participants with identified peripheral neuropathic pain.	
Subject analysis set title	Safety Analysis Set (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety Analysis Set (SAF) was defined and used for all analyses (both safety and efficacy) and it included all patients who received study patch application.	

Primary: Safety (Adverse Events[AE], Serious AEs [SAEs] and Treatment-Emergent AEs [TEAEs]) (SAF)

End point title	Safety (Adverse Events[AE], Serious AEs [SAEs] and Treatment-Emergent AEs [TEAEs]) (SAF)[1]
End point description:	
This endpoint evaluated safety of repeated Qutenza (Capsaicin (8%) high-concentration patch) applications, including the effect in participants diagnosed with different types of PNP. There were 3 deaths reported in the study due to the events of cerebral hemorrhage,pneumonia and squamous cell carcinoma; all events leading to death were not related to Qutenza.	
End point type	Primary
End point timeframe:	
Baseline to End of Treatment (EOT)	

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: Adverse events (AEs) are summarized as counts over the entire study. Statistical analyses was not completed for this endpoint.

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number of participants				
number (not applicable)				
TEAE (Treatment Emergent Adverse Events)	87	62	86	17
Drug-related TEAEs	78	42	73	14
Deaths	2	1	0	0
Serious TEAEs	14	8	13	2

Drug-related serious TEAEs	0	0	0	0
TEAEs leading to discontinuation	5	1	4	1
Drug related TEAEs leading to discontinuation	1	0	1	1
Application site reactions	74	30	68	13

Statistical analyses

No statistical analyses for this end point

Primary: Sensory Testing of most Sensitive Area(s) (Mean value, Area Size per Patch Application) (SAF)

End point title	Sensory Testing of most Sensitive Area(s) (Mean value, Area Size per Patch Application) (SAF)[2]

End point description:

This endpoint was used to complete sensory testing of most sensitive areas to which patches are applied. During this exam participants were assessed on change from the sensory assessments performed at the screening visit. Participants response to warm, cold, sharp (pinprick), vibration sensations, light brush, deep tendon reflexes, most sensitive areas, and allodynia were assesed at each patch application visit. Assessment was performed at week 26 (if applicable), End of Treatment (EOT) and planned or early termination visits. Data was reported for the Week 26, EOT and as a patient mean of all applications.

End point type	Primary

End point timeframe:

Timeframe for this endpoint was by patch application (including last application) from Baseline to End of Treatement (EOT) at each patch application.

Notes:

[2] - 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: Sensory testing of the most sensitive area(s) and the corresponding areas of allodynia was assessed by location counts and absolute value of area size. Statistical analyses was not completed for this endpoint.

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number of participants				
arithmetic mean (standard deviation)				
Screening [N=107;79;98;19]	325.8 (± 239.55)	615.8 (± 395.43)	182.3 (± 180.31)	411.6 (± 324.92)
1st Application [N=107;80;99;20]	327.2 (± 235.22)	606.2 (± 371.64)	192.6 (± 191.65)	456.3 (± 303.77)
2nd Application [N=85;51;76;18]	290.6 (± 206.64)	567.1 (± 344.79)	179.9 (± 208.69)	494.2 (± 327.82)
3rd Application [N=59;29;58;13]	273.1 (± 225.55)	537.7 (± 360.03)	168.8 (± 193.42)	399.2 (± 301.67)
4th Application [N=35;16;39;10]	281.5 (± 190.58)	488.9 (± 330.04)	149 (± 174.56)	335.8 (± 332.57)
5th Application [N=21;8;16;7]	271.7 (± 221.54)	462.4 (± 290.25)	133.2 (± 151.15)	407.1 (± 368.18)

6th Application [N=6;1;6;3]	270.7 (± 286.42)	1626 (± 0)	238.5 (± 254.25)	145.3 (± 59.97)
Last Application [N=107;80;99;20]	307 (± 242.73)	604.6 (± 408.68)	193.9 (± 205.31)	446.6 (± 335.38)
Week 26 [N=107;80;99;20]	288 (± 227.23)	587.6 (± 402.12)	189.9 (± 206.99)	446.6 (± 335.38)
EOT [N=106;80;99;20]	254 (± 225.58)	558.6 (± 406.7)	183.9 (± 198.63)	430.8 (± 368.98)
Patient Mean (All Applications)	294.4 (± 211.97)	586 (± 367.48)	184.5 (± 176.05)	460.9 (± 327.33)

Statistical analyses

No statistical analyses for this end point

Secondary: Neurological Assessment (SAF)

End point title	Neurological Assessment (SAF)

End point description:

An abbreviated neurological examination was performed at the screening visit, at all patch application visits, at week 26 visit (if applicable), and at the planned or early termination visit. It included assessments of gait, muscle strength, and reflexes. The assessments were classified as normal, abnormal-not clinically significant and abnormal-clinically significant. Endpoint of interest was the number and percentage of participants with each neurological assessment score at the different study time points.

End point type	Secondary

End point timeframe:

Baseline (Screening, All Patch application visits, Week 26) to End of Treatment (EOT)

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number of Participants				
number (not applicable)				
Scr Gait Normal [N=106;N=80;N=98;N=20]	100	53	84	17
Scr Gait Abnormal NCS [N=106;N=80;N=98;N=20]	6	16	10	2
Scr Gait Abnormal CS [N=106;N=80;N=98;N=20]	0	11	4	1
Scr Muscle Strength Normal [N=106;N=79;N=99;N=20]	104	66	91	18
Scr Muscle Strength Abn NCS [N=106;N=79;N=99;N=20]	2	9	3	2
Scr Muscle Strength Abn CS [N=106;N=79;N=99;N=20]	0	4	5	0
Scr Reflexes Normal [N=106;N=80;N=99;N=20]	94	32	85	13

Scr Reflexes Abnormal NCS[N=106;N=80;N=99;N=20]	9	26	9	5
Scr Reflexes Abnormal CS[N=106;N=80;N=99;N=20]	3	22	5	2
W26 Gait Normal[N=107;N=80;N=99;N=20]	7	5	4	0
W26 Gait Abnormal NCS[N=107;N=80;N=99;N=20]	0	3	0	0
W26 Gait Abnormal CS[N=107;N=80;N=99;N=20]	0	0	0	0
W26 Muscle Strength Normal[N=107;N=80;N=99;N=20]	7	6	3	0
W26 Muscle Strength Abnor NCS[N=107;N=80;N=99;N=20	0	2	0	0
W26 Muscle Strength Abnor CS[N=107;N=80;N=99;N=20]	0	0	1	0
W26 Reflexes Normal[N=107;N=80;N=99;N=20]	6	4	4	0
W26 Reflexes Abnormal NCS[N=107;N=80;N=99;N=20]	0	4	0	0
W26 Reflexes Abnormal CS[N=107;N=80;N=99;N=20]	1	0	0	0
EOT Gait Normal[N=106;N=80;N=98;N=20]	99	60	88	18
EOT Gait Abnormal NCS[N=106;N=80;N=98;N=20]	7	16	3	2
EOT Gait Abnormal CS[N=106;N=80;N=98;N=20]	0	4	7	0
EOT Muscle Strength Normal[N=106;N=80;N=98;N=20]	104	72	90	19
EOT Muscle Strength Abn NCS[N=106;N=80;N=98;N=20]	2	6	2	1
EOT Muscle Strength Abn CS[N=106;N=80;N=98;N=20]	0	2	7	0
EOT Reflexes Normal[N=106;N=80;N=99;N=20]	95	29	89	14
EOT Reflexes Abn NCS [N=106;N=80;N=99;N=20]	9	38	6	3
EOT Reflexes Abn CS [N=106;N=80;N=99;N=20]	2	13	4	3

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Vital Signs (SAF)

End point title	Change from Baseline Vital Signs (SAF)

End point description:

Before All Applications (Before App) is assessed within 15 minutes prior to application of topical anesthetic and After All Applications (After App) within 5 minutes after patch removal. Sys Blood pressure=Systolic Blood Pressure. Dia Blood Press=Diastolic Blood Pressure. Participants for PHN group Before Subject Mean (all applications) N=106; After Subject Mean (all applications) N=107; Week 26; N=7 and EOT N=107. Participants for HIV-AN group for Before Subject Mean (all applications) N=79; After Subject Mean (all applications) N=79; Week 26; N=9 and EOT N=79. For PNI group Before Subject Mean (all applications) N=99; After Subject Mean (all applications) N=99; Week 26; N=4 and EOT N=99. For "Other" number of participants is as follows Before Subject Mean (all applications) N=20; After Subject Mean (all applications) N=20; Week 26; N=0 and EOT N=20. For group Other (describing other neuropathic pain) Week 26 values are not available for Systolic, Diastolic and Pulse rate.

End point type	Secondary

End point timeframe:

Baseline to End of Treatment (EOT). Vital signs, including BP and PR were measured at screening, at all patch application visits (within 15 min prior to application of topical anesthetic and within 5 min after patch removal) and week 26 visit and EOT.

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number				
arithmetic mean (standard deviation)				
Sys Blood Press [Before App Subject Mean]	-1.9 (± 14.3)	-1.1 (± 14.67)	0.6 (± 11.57)	2.3 (± 16.09)
Sys Blood Press [After App Subject Mean]	6.2 (± 16.54)	-0.3 (± 15.3)	2.2 (± 13.7)	4.4 (± 13.67)
Sys Blood Press Week 26	10.1 (± 10.73)	-9.2 (± 19.41)	0.5 (± 3.32)	0 (± 0)
Sys Blood Press EOT	-1.5 (± 16.89)	-2.2 (± 17.05)	1.4 (± 15.96)	-1.9 (± 18.92)
Dia Blood Press [Before App Subject Mean]	-2.1 (± 9.48)	-1.2 (± 9.24)	0 (± 9.69)	-0.2 (± 9.35)
Dia Blood Press [After App Subject Mean]	1.3 (± 11.06)	0.1 (± 9.1)	0.6 (± 10.36)	2.8 (± 9.43)
Dia Blood Press Week 26	0.9 (± 5.67)	-3.6 (± 15.49)	-1.3 (± 6.75)	0 (± 0)
Dia Blood Press EOT	-1.7 (± 11.35)	-1.9 (± 11.02)	0.4 (± 11.77)	-2.6 (± 10.19)
Pulse Rate [Before App Subject Mean]	-0.3 (± 10.03)	0.1 (± 10.88)	-0.6 (± 8.99)	-1.6 (± 8.17)
Pulse Rate [After App Subject Mean]	-1.6 (± 10.58)	-1.4 (± 9.54)	-0.8 (± 9.8)	-1.8 (± 8.27)
Pulse Rate Week 26	-9.1 (± 10.73)	2.9 (± 11.65)	-5.5 (± 6.66)	0 (± 0)
Pulse Rate EOT	0.1 (± 12.6)	0.6 (± 13.36)	1.9 (± 11.18)	-1.7 (± 10.59)

Statistical analyses

No statistical analyses for this end point

Secondary: Dermal Assessment at Patch Applications (SAF)

End point title	Dermal Assessment at Patch Applications (SAF)

End point description:

Dermal assessment was done at patch applications to determine if there were any signs of irritation.It was completed at all patch application visits (prior to application of topical anesthetic, within 5 min and 60 min after patch removal), at week 26 visit (if applicable), and at the EOT or early termination visits. Scale for assessment was based on a 0 to 7 point severity score. The endpoints of interest were counts by category as listed; [No evidence of irritation], [Minimal erythema barely perceptive],[Definite erythema, readily visible; minimal and edema or minimal popular response],[Erythema and papules],[Definite edema],[Erythema, edema, and papules],[Vesicular eruption],[Strong reaction spreading beyond test site] and [Combined category >= 4 (definite edema or higher)].

End point type	Secondary

End point timeframe:

Baseline to End of Treatment (EOT).

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number of Participants				
number (not applicable)				
1st App Before anesthetic[Combined category >=4]	0	0	0	0
1st App 5min after patch[Combined category >= 4]	6	2	5	0
1st App 60min after patch[Combined category >= 4]	5	1	4	0
2nd App Before anesthetic[Combined category >= 4]	0	0	0	0
2nd App 5min after patch[Combined category >= 4]	6	0	3	0
2nd App 60min after patch[Combined category >= 4]	3	1	4	0
3rd App Before anesthetic[Combined category >= 4]	0	0	0	0
3rd App 5min after patch[Combined category >= 4]	1	0	2	0
3rd App 60min after patch[Combined category >= 4]	1	0	1	0
4th App Before anesthetic[Combined category >= 4]	0	0	0	0
4th App 5min after patch[Combined category >= 4]	0	0	1	0
4th App 60min after patch[Combined category >= 4]	0	0	0	0
5th App Before anesthetic[Combined category >= 4]	0	0	0	0
5th App 5min after patch[Combined category >= 4]	0	0	0	0
5th App 60min after patch[Combined category >= 4]	0	0	0	0
6th App Before anesthetic[Combined category >= 4]	0	0	0	0
6th App 5min after patch[Combined category >= 4]	0	0	0	0
6th App 60min after patch[Combined category >= 4]	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Brief Pain Inventory Question 5 (average pain)(SAF)

End point title	Change from Baseline Brief Pain Inventory Question 5 (average pain)(SAF)

End point description:

Responses to BPI Question 5 (average pain) were recorded daily and weekly (± 2 days) from the 1st patch application until the planned or early termination visit. Weekly response was recorded on the day chosen by patient during the 1st patch application visit (± 2 days). Each BPI item uses a 0 to 10 rating scale anchored at zero for"no pain"and 10 for "pain as bad as you can imagine" for severity and "does not interfere" to "completely interferes" for interference. Number of participants for each month was as follows; Month 1[N=106;79;99;20]; Month 2[N=102;69;95;19];Month 3[N=97;65;89;18];Month 4[N=91;64;89;18];Month 5[N=90;58;79;18];Month 6[N=81;59;77;16];Month 7[N=79;58;72;15]; Month 8[N=75;56;69;15]; Month 9[N=70;49;69;14]; Month 10[N=70;47;64;12]; Month 11[N=68;43;60;11]; Month 12[N=63;42;58;11];Month 13[N=54;41;49;9];Month 14[N=42;29;44;5]; Month 15[N=23;21;25;3]; Month 16[N=8;6;3;2]; Month 17[N=2;2;1;1]; Month 18[N=1;0;1;1]; Month 19[N=1;0;1;0];Month 20[N=1;0;0;0].

End point type	Secondary

End point timeframe:

Baseline to End of Treatment (EOT).

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number of Participants				
arithmetic mean (standard deviation)				
Month 1 Post-baseline	-0.9 (± 1.25)	-0.7 (± 1.3)	-1.1 (± 1.49)	-0.6 (± 1.07)
Month 2 Post-baseline	-1 (± 1.41)	-1.1 (± 1.52)	-1.3 (± 1.89)	-0.7 (± 0.96)
Month 3 Post-baseline	-1 (± 1.35)	-1 (± 1.57)	-1.3 (± 1.69)	-0.7 (± 1.06)
Month 4 Post-baseline	-1.3 (± 1.54)	-1.3 (± 1.96)	-1.6 (± 1.71)	-0.9 (± 1.12)
Month 5 Post-baseline	-1.4 (± 1.51)	-1.3 (± 1.81)	-1.6 (± 1.93)	-1 (± 1.36)
Month 6 Post-baseline	-1.4 (± 1.61)	-1.1 (± 1.83)	-1.9 (± 1.89)	-0.8 (± 1.05)
Month 7 Post-baseline	-1.5 (± 1.76)	-1.2 (± 1.86)	-2 (± 1.89)	-0.9 (± 1.32)
Month 8 Post-baseline	-1.6 (± 1.75)	-1.2 (± 1.74)	-2.2 (± 2.04)	-1.3 (± 1.46)
Month 9 Post-baseline	-1.5 (± 1.99)	-1.2 (± 1.75)	-2 (± 2.12)	-1.5 (± 1.34)
Month 10 Post-baseline	-1.6 (± 1.96)	-1.3 (± 1.58)	-1.9 (± 2.06)	-1.7 (± 1.71)
Month 11 Post-baseline	-1.7 (± 2.01)	-1.5 (± 1.62)	-2 (± 2.21)	-1.4 (± 1.67)
Month 12 Post-baseline	-1.7 (± 1.92)	-1.5 (± 1.83)	-2.3 (± 2.19)	-2.1 (± 1.56)
Month 13 Post-baseline	-1.8 (± 1.87)	-1.8 (± 2.09)	-2.3 (± 2.23)	-2.2 (± 1.85)
Month 14 Post-baseline	-1.6 (± 1.96)	-1.5 (± 1.72)	-2.1 (± 2.47)	-2.5 (± 2.17)
Month 15 Post-baseline	-1.6 (± 2.32)	-1.9 (± 1.66)	-1.7 (± 2.09)	-0.8 (± 1.45)
Month 16 Post-baseline	-2.6 (± 2.04)	-2.3 (± 2.69)	0.6 (± 0.93)	-1.8 (± 0.71)
Month 17 Post-baseline	-1.8 (± 2.21)	-0.9 (± 0.09)	-0.3 (± 99999)	-2.9 (± 99999)
Month 18 Post-baseline	-2.8 (± 99999)	0 (± 0)	0.2 (± 99999)	-2.9 (± 99999)
Month 19 Post-baseline	-3.6 (± 99999)	0 (± 0)	0.2 (± 99999)	0 (± 99999)
Month 20 Post-baseline	-3 (± 99999)	0 (± 0)	0 (± 0)	0 (± 0)

Statistical analyses

No statistical analyses for this end point

Secondary: Tolerability of patch application (SAF)

End point title	Tolerability of patch application (SAF)

End point description:

Analyses of tolerability include summaries of the percent of intended patch application time overall and by patients' individual neuropathic diagnosis. Duration of patch application was the difference between the stop and start times, and it was presented as a percentage of intended patch application duration. The proportion of patients completing at least 90% of the intended patch application were reported at each patch application. Additionally, a patient was deemed to have had an early patch removal if they had an AE with study drug action of temporary discontinuation, if the patch application duration was less than 100%, or if the patient went on to receive additional subsequent patch applications.

End point type	Secondary

End point timeframe:

Duration of patch application was the difference between the stop and start times.

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number				
arithmetic mean (standard deviation)				
Time to 2nd patch application(days)[N=85;51;76;18]	98.3 (± 49.79)	111.1 (± 43.57)	94.8 (± 47.02)	84.3 (± 24.62)
Time to 3rd patch application(days)[N=59;29;58;13]	103.3 (± 40.94)	127.3 (± 55.56)	107.9 (± 44.87)	104.8 (± 28.7)
Time to 4th patch application(days)[N=35;16;39;10]	94.7 (± 29.08)	110.1 (± 35.61)	103.8 (± 28.19)	80 (± 12.78)
Time to 5th patch application(days)[N=21;8;16;7]	89.8 (± 22.06)	79.4 (± 7.91)	83.3 (± 19.38)	74.4 (± 12.42)
Time to 6th patch application(days)[N=6;1;6;3]	85 (± 32.54)	91 (± 0)	74.8 (± 10.98)	70 (± 10.39)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline Brief Pain Inventory (BPI) Question 6 (pain now)(SAF)

End point title	Change from Baseline Brief Pain Inventory (BPI) Question 6 (pain now)(SAF)

End point description:

Brief Pain Inventory (BPI) Question 6 (pain now) was used to assess participants pain now. Participants completed questionaire with numeric rating scale measuring severity of pain and its interference with daily function on a 0-10 rating scale,using 0 to identify "no pain" and 10 "pain as bad as you can imagine". Data reported is subject mean of all applications before each patch application and to within 5 min and after 1 hour after each patch application.

End point type	Secondary

End point timeframe:

Response to BPI Question 6 (pain now) was recorded before topical anesthetic application, within 5 min following patch removal, and after 1 hour following patch removal.

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number				
arithmetic mean (standard deviation)				
Subject Mean All Applications [Prior to patch]	-0.5 (± 1.15)	-0.2 (± 0.83)	-0.4 (± 0.85)	-0.2 (± 1.18)
Subject Mean All Applications [5 min after patch]	0.6 (± 2.28)	-0.7 (± 2.35)	-0.3 (± 2.32)	-0.6 (± 1.54)
Subject Mean All Applications [1 hour after patch]	-0.7 (± 2.2)	-1 (± 2.3)	-1 (± 2.22)	-1 (± 1.57)

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change (PGIC) for combined category of very much improved + much improved + minimally improved (SAF)

End point title	Patient Global Impression of Change (PGIC) for combined category of very much improved + much improved + minimally improved (SAF)

End point description:

The Patient Global Impression of Change (PGIC) is a patient-rated instrument that measures change in participants overall status on a 7-point scale ranging from 1 (very much improved) to 7 (very much worse). Data reported is the precentage of participants who reported improvement in their overall status (combined category of very much improved + much improved + minimally improved) for each application. Participants answered a PGIC questionnaire at patch application visits (except 1st patch application visit) and 4 weeks after each patch application visit, at week 26 visit (if applicable), and at the planned or early termination visit.

End point type	Secondary

End point timeframe:

Baseline to End of Treatment (EOT). Safety Analysis Set (SAF).

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20

Units: percent				
number (not applicable)				
1st App [4 weeks after]	61.5	54.5	67.4	47.1
2nd App [Prior to patch application]	47.9	55.3	68.3	50
2nd App [4 weeks after]	67.7	76.9	81.5	69.2
3rd App [Prior to patch application]	80.9	70.8	73.5	75
3rd App [4 weeks after]	69	75	73.3	72.7
4th App [Prior to patch application]	66.7	100	83.3	88.9
4th App [4 weeks after]	80	91.7	71.9	87.5
5th App [Prior to patch application]	94.7	88.9	80	83.3
5th App [4 weeks after]	87.5	85.7	66.7	83.3
6th App [Prior to patch application]	80	0	66.7	66.7
6th App [4 weeks after]	100	0	60	66.7
Last App [Prior to patch application]]	57.9	65.1	70.8	71.4
Last App [4 weeks after]	57.7	53.8	65.4	52.9

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline EQ-5D VAS Questionnaire (SAF)

End point title	Change from Baseline EQ-5D VAS Questionnaire (SAF)

End point description:

The EQ-5D is used as a measure of participants health-related quality of life (HRQoL) on a visual analog scale (VAS) on a graduated (0 to 100) scale, with higher scores for higher HRQoL.The EQ-5D self-reported questionnaire includes a VAS, which records the respondent's self-rated health status on a graduated (0 to 100) scale, with higher scores for higher HRQoL. It also includes the EQ-5D descriptive system, which comprises 5 dimensions of health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each of the 5 dimensions is assessed in 3 levels: "no problems", "some problems", or "extreme problems/unable to perform activity". Data represented is the subject mean of all applications from Baseline to EOT.

End point type	Secondary

End point timeframe:

Baseline to End of Treatment [EOT]

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number				
arithmetic mean (standard deviation)				
All App[Prior to Patch App N=74 N=39 N=66 N=14]	0.3 (± 18.2)	3.4 (± 16.16)	-1.8 (± 15.2)	0.1 (± 10.82)
All App[4 Weeks After N=86 N=55 N=86 N=16]	1.9 (± 24.71)	3 (± 31.75)	1.9 (± 24.02)	-2.2 (± 14.75)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline HADS (Hospital Anxiety and Depression Scale)(SAF)

End point title	Change from Baseline HADS (Hospital Anxiety and Depression Scale)(SAF)

End point description:

The HADS is a self-report scale developed for the assessment of anxiety and depression in non-psychiatric populations. In this study it was used to screen for the presence of moderate to severe depressive symptomatology and to assess co-morbid depression during the course of the study. It contains 14 items rated on a 4-point Likert-type scale. There are 2 sub-scales, one assessing depression and the other anxiety. The 7-item depression and anxiety subscales yield scores of 0 to 21 that are interpreted with the following cut-off points: 0 to 7, normal; 8 to 10, mild mood disturbance; 11 to 14, moderate mood disturbance; and 15 to 21, severe mood disturbance. Full Analysis Set (FAS) was used for analysis and data presented represents change from baseline.

End point type	Secondary

End point timeframe:

Baseline to End of Treatment [EOT}.

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number				
arithmetic mean (standard deviation)				
1st App 4 weeks after[N=82;51;84;15]	-0.5 (± 3.28)	0.6 (± 3.57)	-0.5 (± 2.97)	-0.7 (± 2.94)
2nd App Prior to patch[N=72;34;60;14]	-1.1 (± 2.82)	-0.7 (± 3.01)	-0.6 (± 3.07)	-2.1 (± 2.4)
2nd App 4 weeks after[N=60;24;54;13]	-0.8 (± 3.16)	-0.3 (± 3.43)	-1.3 (± 3.13)	-1.8 (± 2.62)
3rd App Prior to patch[N=46;21;49;11]	-0.7 (± 2.99)	-0.2 (± 2.68)	-1 (± 3.11)	-1.5 (± 2.77)
3rd App 4 weeks after[N=43;13;44;11]	-0.6 (± 2.95)	-0.9 (± 3.8)	-0.9 (± 3.37)	-1 (± 3.1)
4th App Prior to patch[N=30;11;36;8]	-1.1 (± 3.03)	-2.3 (± 3.2)	-1.6 (± 3.21)	-1.1 (± 2.1)
4th App 4 weeks after[N=24;12;33;8]	-0.3 (± 3.03)	-0.3 (± 3.98)	-0.7 (± 2.8)	-0.5 (± 1.6)
5th App Prior to patch[N=19;8;16;5]	-1.3 (± 3.07)	0.5 (± 4.21)	-1.6 (± 3.61)	-0.6 (± 1.67)
5th App 4 weeks after[N=16;7;12;6]	-1.3 (± 2.89)	0.7 (± 4.5)	-0.7 (± 4.01)	-1.7 (± 3.39)
6th App Prior to patch[N=5;0;6;3]	-0.4 (± 4.56)	0 (± 0)	2.5 (± 3.02)	-1.3 (± 2.89)
6th App 4 weeks after[N=4;0;5;3]	-1.8 (± 3.86)	0 (± 0)	1.2 (± 4.02)	-1.3 (± 0.58)
Last App Prior to patch[N=73;38;64;13]	-0.6 (± 2.91)	-0.7 (± 2.78)	-1 (± 3.45)	-1.5 (± 2.4)
Last App 4 weeks after[N=74;47;78;16]	-0.5 (± 3.27)	-0.1 (± 3.5)	-0.8 (± 3.54)	-1 (± 3.16)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline WPAI:NP (Work Productivity and Activity Impairment Questionnaire)Items 2-6 Scores(SAF)

End point title	Change from Baseline WPAI:NP (Work Productivity and Activity Impairment Questionnaire)Items 2-6 Scores(SAF)

End point description:

The WPAI:NP is a self-report scale developed for the assessment of work productivity and activity impairment related to neuropathic pain. It contains 6 items. The 1st item asks if the patient is currently working. Items 2 to 4 ask for responses in terms of the number of hours during the past 7 days associated with various activities. Items 5 and 6 are rated on a 10-point Likert-type scale ranging from "problem had no effect on my work/daily activities" to "problem completely prevented me from doing my work/daily activities". Safety Analysis Set (SAF) was used for analysis and data represented shows change from baseline represented as subject mean of all applications to questions 2-6.

End point type	Secondary

End point timeframe:

Baseline to End of Treatment [EOT].

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number				
arithmetic mean (standard deviation)				
Q2 Mean All App Prior to patch[N=6;11;27;5]	-5 (± 10.61)	-4 (± 9.66)	-1.4 (± 8.69)	6.5 (± 6.59)
Q2 Mean All App 4 weeks after [N=8;15;34;5]	-1.4 (± 12.56)	4.6 (± 37.99)	-1.2 (± 14.21)	5.7 (± 8.69)
Q3 Mean All App Prior to patch[N=6;11;27;5]	-2 (± 15.27)	-0.5 (± 1.98)	-1.2 (± 6.6)	3 (± 6.71)
Q3 Mean All App 4 weeks after[N=8;15;34;5]	-0.9 (± 17.32)	3.9 (± 14.59)	4.6 (± 16.8)	5.8 (± 6.52)
Q4 Mean All App Prior to patch[N=6;11;27;5]	-1.8 (± 17.15)	-3.7 (± 14.92)	1.9 (± 9.79)	2.3 (± 3.72)
Q4 Mean All App 4 weeks after[N=8;15;34;5]	4.1 (± 12.76)	-6.9 (± 24.01)	-2.2 (± 20.98)	4 (± 14.25)
Q5 Mean All App Prior to patch[N=6;8;23;4]	-0.9 (± 0.82)	-0.4 (± 0.65)	-0.7 (± 1.26)	-1.3 (± 1.7)
Q5 Mean all App 4 weeks after[N=8;12;27;4]	-0.6 (± 0.71)	-0.9 (± 1.29)	-0.8 (± 1.74)	-1.8 (± 3.25)
Q6 Mean All App Prior to patch[N=74;39;66;14]	-0.6 (± 1.59)	-0.6 (± 1.1)	-0.8 (± 1.41)	-0.6 (± 0.97)

Q6 Mean All App 4 weeks after[N=86;55;86;16]	-0.5 (± 2.44)	-0.9 (± 1.76)	-1.2 (± 2.27)	-0.8 (± 1.33)

Statistical analyses

No statistical analyses for this end point

Secondary: Self-assessment of Treatment (SAT) (SAF)

End point title	Self-assessment of Treatment (SAT) (SAF)

End point description:

Participants answered a SAT questionnaire at week 26 (if applicable) and the planned or early termination visit. The SAT assesses treatment satisfaction by using a 5-point Likert-type scale ranging from -2 (a strong negative response) to 2 (a strong positive response); zero indicates a neutral response. The questionnaire contains each of the following questions: 1. How do you assess your pain level after treatment in this study? 2. How do you assess your activity level after treatment in this study? 3. How has your quality of life changed after treatment in this study? 4. Would you undergo this treatment again? 5. How do you compare the treatment you received in this study to previous medication or therapies for your pain?. Data was represented by counts in combined categories [Worse: (-2) + (-1)] [Not Better or Worse: (-2) + (-1) + (0)] and [Better: (1) + (2).

End point type	Secondary

End point timeframe:

Baseline to End of Treatment (EOT)

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number of participants				
number (not applicable)				
Pain Level [Worse] [N=71;48;65;17]	7	6	10	2
Pain Level [Not Better or Worse] [N=71;48;65;17]	26	20	23	8
Pain Level [Better] [N=71;48;65;17]	38	22	32	7
Activity Level [Worse] [N=71;48;65;17]	13	10	12	2
Activity Level[Not Better or Worse][N=71;48;65;17]	38	23	34	10
Activity Level [Better] [N=71;48;65;17]	20	15	19	5
Quality of Life[Worse][N=71;48;65;17]	6	5	6	0
Quality of Life[Not Better orWorse][N=71;48;65;17]	40	27	28	11
Quality of Life[Better][N=71;48;65;17]	25	16	31	6
Treatment again[Worse][N=71;48;65;17]	22	16	22	9
Treatment again[Not Better orWorse][N=71;48;65;17]	14	7	10	0
Treatment again[Better][N=71;48;65;17]	35	25	33	8

Compare treatment[Worse][N=71;48;65;17]	15	8	15	4
Compare treatment[Not Better Worse][N=71;48;65;17]	24	20	14	7
Compare treatment[Better][N=71;48;65;17]	32	20	36	6

Statistical analyses

No statistical analyses for this end point

Secondary: Use of Concomitant Pain Medication following Patch Application(SAF)

End point title	Use of Concomitant Pain Medication following Patch Application(SAF)

End point description:

Concomitant medication use was assessed throughout the study, from Baseline to End of Treatment or early termination visit. Classes of interest were: chronic medication for neuropathic pain, antidepressants, antiepileptic drugs, and opioids. Data presented reflects concomitant medication post-application used on days 1 through 5 after patch application.

End point type	Secondary

End point timeframe:

Baseline to End of Treatment[EOT]

End point values	PHN [Post-herpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-traumatic Nerve Injury]	Other type of Peripheral Neuropathic Pain [PNP]
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	80	99	20
Units: Number of Participants				
number (not applicable)				
ANALGESICS	42	23	36	5
ANESTHETICS	4	1	5	0
ANTIEPILEPTICS	1	1	0	0
ANTIHISTAMINES FOR SYSTEMIC USE	1	1	0	0
ANTIINFLAMMATORY AND ANTIRHEUMATIC	11	2	8	0
ANTIPRURITICS, INCL ANTIHISTAMINES, ANESTHETICS	0	1	0	0
CARDIAC THERAPY	3	3	2	0
COUGH AND COLD PREPARATIONS	0	4	1	0
DRUGS FOR CONSTIPATION	3	1	0	0
EMOLLIENTS AND PROTECTIVES	3	1	0	0
OPHTHALMOLOGICALS	8	1	6	0
OTHER DERMATOLOGICAL PREPARATIONS	7	1	6	0
OTHER GYNECOLOGICALS	3	2	2	0
OTOLOGICALS	0	1	0	0
STOMATOLOGICAL PREPARATIONS	10	1	6	0

THROAT PREPARATIONS	0	1	0	0
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	10	2	8	0
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	3	1	0	0
UROLOGICALS	0	1	0	0
VASOPROTECTIVES	0	1	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) are summarized as counts over the entire study and by patch application. Within each of these time periods AEs are summarized overall and by individual neuropathic diagnosis. Only TEAEs were analyzed in this study.

Adverse event reporting additional description:

Each AE was categorized based on which patch applications it occurred between (i.e.,between 1st and 2nd, between 2nd and 3rd, etc., or after last). Each AE was additionally categorized based on whether it occurred within 7 days after a patch application, and also based on whether it occurred more than 7 days after a patch application.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1.

Reporting groups

Reporting group title	PHN [Postherpetic Neuralgia]
Reporting group description: -	
Reporting group title	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]
Reporting group description: -	
Reporting group title	PNI [Post-Traumatic Nerve Injury]
Reporting group description: -	
Reporting group title	Other type of Peripheral Neuropathic Pain [PNP]

Reporting group description: -

Serious adverse events	PHN [Postherpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-Traumatic Nerve Injury]
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 107 (13.08%)	8 / 80 (10.00%)	13 / 99 (13.13%)
number of deaths (all causes)	2	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell unclassifiable lymphoma high grade			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	2 / 107 (1.87%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Squamous cell carcinoma			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Chemotherapy			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip arthroplasty			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip surgery			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spinal laminectomy			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Biopsy			

subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biopsy bone			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	2 / 107 (1.87%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Complex regional pain syndrome			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuralgia			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal ulcer haemorrhage			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			

subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Bladder disorder			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Mobility decreased			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muskuloskeletal chest pain			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIV peripheral neuropathy			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 107 (0.00%)	2 / 80 (2.50%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 107 (0.93%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral pericarditis			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Other type of Peripheral Neuropathic Pain [PNP]		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 20 (10.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell unclassifiable lymphoma high grade			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral ischaemia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Chemotherapy			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip arthroplasty			

subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip surgery				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Knee arthroplasty				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal laminectomy				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				

subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Biopsy			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Biopsy bone			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar vertebral fracture			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Bradycardia			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular tachycardia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Complex regional pain syndrome			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuralgia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Partial seizures			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Abdominal pain upper				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal ulcer haemorrhage				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Bladder disorder				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal colic				

subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fistula			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mobility decreased			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muskuloskeletal chest pain			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Gastroenteritis				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
HIV peripheral neuropathy				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral pericarditis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	PHN [Postherpetic Neuralgia]	HIV-AN [Human Immunodeficiency Virus-associated Neuropathy]	PNI [Post-Traumatic Nerve Injury]
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 107 (71.96%)	44 / 80 (55.00%)	76 / 99 (76.77%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 107 (5.61%)	1 / 80 (1.25%)	3 / 99 (3.03%)
occurrences (all)	8	1	3
Surgical and medical procedures			
Haemangioma removal			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Application site erythema			
subjects affected / exposed	24 / 107 (22.43%)	2 / 80 (2.50%)	19 / 99 (19.19%)
occurrences (all)	42	3	42
Application site pain			
subjects affected / exposed	46 / 107 (42.99%)	21 / 80 (26.25%)	40 / 99 (40.40%)
occurrences (all)	110	34	92
Influenza like illness			

subjects affected / exposed	1 / 107 (0.93%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences (all)	1	1	0
Pain			
subjects affected / exposed	13 / 107 (12.15%)	6 / 80 (7.50%)	16 / 99 (16.16%)
occurrences (all)	29	6	35
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 107 (0.93%)	4 / 80 (5.00%)	2 / 99 (2.02%)
occurrences (all)	1	4	2
Psychiatric disorders			
Middle insomnia			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Investigations			
Biopsy skin			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences (all)	0	1	0
Blood iron decreased			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Muscle strain			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Allodynia			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Burning sensation			
subjects affected / exposed	11 / 107 (10.28%)	8 / 80 (10.00%)	20 / 99 (20.20%)
occurrences (all)	29	13	51
Dizziness			

subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
subjects affected / exposed	4 / 107 (3.74%)	1 / 80 (1.25%)	6 / 99 (6.06%)
occurrences (all)	5	1	7
Paraesthesia			
subjects affected / exposed	0 / 107 (0.00%)	2 / 80 (2.50%)	1 / 99 (1.01%)
occurrences (all)	0	2	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	3 / 99 (3.03%)
occurrences (all)	0	0	3
Abdominal pain upper			
subjects affected / exposed	0 / 107 (0.00%)	1 / 80 (1.25%)	0 / 99 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 107 (3.74%)	1 / 80 (1.25%)	8 / 99 (8.08%)
occurrences (all)	5	1	8
Vomiting			
subjects affected / exposed	2 / 107 (1.87%)	1 / 80 (1.25%)	2 / 99 (2.02%)
occurrences (all)	3	1	2
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	29 / 107 (27.10%)	1 / 80 (1.25%)	29 / 99 (29.29%)
occurrences (all)	79	1	77
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 107 (2.80%)	0 / 80 (0.00%)	3 / 99 (3.03%)
occurrences (all)	3	0	4
Back pain			

subjects affected / exposed	3 / 107 (2.80%)	4 / 80 (5.00%)	2 / 99 (2.02%)
occurrences (all)	3	4	2
Pain in extremity			
subjects affected / exposed	2 / 107 (1.87%)	11 / 80 (13.75%)	5 / 99 (5.05%)
occurrences (all)	2	19	7
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 107 (1.87%)	0 / 80 (0.00%)	2 / 99 (2.02%)
occurrences (all)	2	0	2
Influenza			
subjects affected / exposed	2 / 107 (1.87%)	0 / 80 (0.00%)	7 / 99 (7.07%)
occurrences (all)	2	0	8
Laryngitis			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 107 (1.87%)	0 / 80 (0.00%)	4 / 99 (4.04%)
occurrences (all)	2	0	5
Metabolism and nutrition disorders			
Folate deficiency			
subjects affected / exposed	1 / 107 (0.93%)	0 / 80 (0.00%)	1 / 99 (1.01%)
occurrences (all)	1	0	1
Vitamin B12 deficiency			
subjects affected / exposed	0 / 107 (0.00%)	0 / 80 (0.00%)	0 / 99 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Other type of Peripheral Neuropathic Pain [PNP]		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 20 (85.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Haemangioma removal			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Application site erythema			
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	10		
Application site pain			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	15		
Influenza like illness			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	8 / 20 (40.00%)		
occurrences (all)	16		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Middle insomnia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Investigations			
Biopsy skin			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Blood iron decreased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Muscle strain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nervous system disorders			
Allodynia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Burning sensation			
subjects affected / exposed	6 / 20 (30.00%)		
occurrences (all)	12		
Dizziness			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Neuralgia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorder			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	6		
Vomiting			

subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 3		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	 3 / 20 (15.00%) 10		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 2 1 / 20 (5.00%) 1		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Laryngitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 0 / 20 (0.00%) 0 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		
Metabolism and nutrition disorders Folate deficiency subjects affected / exposed occurrences (all) Vitamin B12 deficiency subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The original study protocol for this study was dated 30 Apr 2010. There were 4 non-substantial amendments to the study protocol, dated 22 Oct 2010, 01 Mar 2011, 02 Dec 2011, and 28 May 2013.

Notes: