ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 02/25/2016

ClinicalTrials.gov ID: NCT00983385

Study Identification

Unique Protocol ID:	787579
Brief Title:	Evaluation of Effectiveness and Tolerability of Tapentadol Hydrochloride in Subjects With Severe Chronic Low Back Pain Taking Either WHO Step I or Step II Analgesics or no Regular Analgesics
Official Title:	An Evaluation of the Effectiveness and Tolerability of Tapentadol Hydrochloride Prolonged Release, and Tapentadol Hydrochloride Immediate Release on Demand, in Subjects With Uncontrolled Severe Chronic Nociceptive, Mixed or Neuropathic Low Back Pain Taking Either WHO Step I or Step II Analgesics or no Regular Analgesics.
Secondary IDs:	2009-010427-12 [EudraCT Number]

Study Status

Record Verification:	February 2016
Overall Status:	Completed
Study Start:	September 2009
Primary Completion:	May 2010 [Actual]
Study Completion:	July 2010 [Actual]

Sponsor/Collaborators

Sponsor:	Grünenthal GmbH
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?: No

IND/IDE Protocol?: No

Review Board: Approval Status: Approved
Approval Number: 08/17/2009
Board Name: Comite de Protection des Personnes Ile de France VI
Board Affiliation: Ministry of Health and Solidarity
Phone: +33 01 42 16 16 83
Email:

Data Monitoring?: No

Plan to Share Data?:

Oversight Authorities: France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
United Kingdom: Medicines and Healthcare Products Regulatory Agency
Spain: Agencia Española de Medicamentos y Productos Sanitarios
Austria: Federal Ministry for Health and Women
Germany: Federal Institute for Drugs and Medical Devices
Switzerland: Swissmedic
Poland: The Central Register of Clinical Trials

Study Description

Brief Summary: The main objective of the study is to evaluate the effectiveness, tolerability, and safety of tapentadol hydrochloride prolonged release in subjects suffering from severe chronic low back pain (LBP) who are taking either WHO Step I or Step II analgesics or no regular analgesics. This is a clinical effectiveness trial designed to establish a link between anticipated clinical outcomes and the clinical practice by means of selected measures of clinical and subject-reported outcome.

The trial will compare the effectiveness of previous analgesic treatment (either WHO Step I or Step II analgesics or no regular analgesics) with that of tapentadol hydrochloride prolonged release (PR) treatment during defined periods of evaluation.

Detailed Description:

Conditions

Conditions: Chronic Pain
Low Back Pain

Keywords: low back pain
pain
assessment
tapentadol

centrally acting analgesic

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	N/A
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	208 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Tapentadol Tapentadol PR was given orally twice a day. A maximum of 2 oral Tapentadol IR tablets per day, with a minimum of a 4 hour interval between doses, were taken if there were acute pain episodes. The total daily dose of Tapentadol PR and IR were not permitted to exceed 500 mg per day.	Drug: Tapentadol PR Tapentadol Prolonged Release (PR) Titration and Optimal Dose Period: Starting at 50 mg Tapentadol PR twice daily, adjusting at 50 mg PR steps (upwards or downwards) as necessary to achieve a balance between pain relief and a satisfactory level of tolerability. Participants were not permitted to exceed 500 mg of Tapentadol per day. Other Names: • Palexia® • Nucynta® Observation period Eligibilty assessment period to characterize the baseline over a one week period (week -1). Participants continued their previous treatment prior to allocation to tapentadol, if eligible. Drug: Tapentadol PR Maintenance Period: In this period participants continued Tapentadol Prolonged Release (PR) on the dose established in the Titration and Optimal Dose Period. Tapentadol IR Participants were not permitted to exceed 500 mg of Tapentadol per day. Other Names: • Palexia®

Arms	Assigned Interventions
	• Nucynta®

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Participants must have signed an Informed Consent Form.
- Participants were men or non-pregnant, non-lactating women. Female participants must be postmenopausal, surgically sterile, or practicing an effective method of birth control. Women of childbearing potential must have a negative pregnancy test at screening.
- Participants must be appropriately communicative to verbalize and to differentiate with regard to location and intensity of the pain.
- Participants must be at least 18 years of age.
- Participants must have a diagnosis of chronic low back pain; chronic pain defined as pain lasting for at least 3 months.
- If the participant has radicular pain, this must have been present for at least 3 months and stable for the 4 weeks before enrollment.
- Participants's pain must require a strong analgesic (defined as WHO Step III) as judged by the Investigator.
- Participants must report a rate of satisfaction with their previous analgesic regimen not exceeding "fair" on a subject satisfaction with treatment scale (5-point VRS).
- If under regular, daily pretreatment:
    - Participants must be taking a WHO Step I or Step II analgesic medication on a daily basis for at least 2 weeks prior to the Screening Visit.
    - The Investigator considers dose increase of WHO Step I analgesics (as mono- or combination therapy) and/or continuation with or dose increase of WHO Step II analgesics inadequate for the individual participant, whatever applicable.
    - Participants must have an average pain intensity score (NRS 3) greater than 5 points during the last 3 days prior to the Screening Visit. or
- If no regular analgesic pretreatment is reported:
    - Participants must have an average pain intensity score (NRS-3) greater than 6 points in the last 3 days prior to the Screening Visit and related to low back pain.

Exclusion Criteria:

- Presence of a clinically significant disease or laboratory findings that in the Investigator's opinion may affect efficacy or safety assessments.
- Presence of active systemic or local infection that may, in the opinion of the Investigator, affect the efficacy, quality of life/ function or safety assessments.
- History of alcohol or drug abuse, or suspicion of in Investigator's judgement.
- Presence of concomitant autoimmune inflammatory conditions.
- Known history of or laboratory values reflecting severe renal impairment.
- Known history of moderately or severely impaired hepatic function.
- History of or active hepatitis B or C within the past 3 months or history of HIV infection
- History of seizure disorder or epilepsy.
- Any of the following within 1 year: mild/moderate traumatic brain injury, stroke, transient ischemic attack, or brain neoplasm. Severe traumatic brain injury within 15 years (consisting of 1 or more of the following: brain contusion, intracranial hematoma, either unconsciousness or post-traumatic amnesia lasting more than 24 h) or residual sequelae suggesting transient changes in consciousness.
- Pregnant or breast-feeding.
- History of allergy to, or hypersensitivity to tapentadol hydrochloride or its excipients, or contraindications related to tapentadol hydrochloride including:
    - Participants with acute or severe bronchial asthma or hypercapnia.
    - Participants who have or are suspected of having paralytic ileus.
- Employees of the Investigator or trial site, with direct involvement in this trial or other trials under the direction of the Investigator or trial site, as well as family members of employees of the Investigator.
- Participation in another trial concurrently or within 4 weeks prior to the Screening Visit.
- Known to or suspected of not being able to comply with the protocol and the use of the investigational medicinal product.
- Use of monoamine oxidase inhibitors within 14 days before the Screening Visit.
- Non-stable dosing of selective serotonin reuptake inhibitors within 30 days before the Screening Visit (the doses must remain stable during the trial).
- Presence of conditions other than low back pain that could confound the assessment or self evaluation of pain, e.g., anatomical deformities, significant skin conditions such as abscess or syndromes with widespread pain such as fibromyalgia.
- Any concomitant painful condition that could interfere with the subject's trial assessments or with their ability to differentiate low back pain from other painful conditions.
- Any painful procedures during the trial (e.g., major surgery) that may, in the opinion of the Investigator, affect the efficacy or safety assessments.
- Pending litigation due to chronic pain or disability.
- Intake of Step III analgesics within the 30 days prior to the Screening Visit.

Contacts/Locations

Study Officials: Hans Kress, Prof. MD
Study Principal Investigator
Medical University / AKH Vienna

Locations: Austria

Site 5
Graz, Austria

Site 1
Vienna, Austria

Site 2
Vienna, Austria

Site 3
Vienna, Austria

Site 4
Vienna, Austria

Croatia
Site 3
Karlovac, Croatia

Site 2
Opatija, Croatia

Site 1
Sisak, Croatia

France
Site 2
Chateaugiron, France

Site 4
La Seyne sur Mer, France

Site 3
Murs Erigné, France

Site 1
Paris, France

Germany
Site 3
Berlin, Germany

Site 7
Böblingen, Germany

Site 4

Celle, Germany

Site 1
Dresden, Germany

Site 6
Hannover, Germany

Site 5
Lünen, Germany

Site 2
Wiesbaden, Germany

Italy
Site 6
Bologna, Italy

Site 5
Catania, Italy

Site 2
Genova, Italy

Site 4
Parma, Italy

Site 3
Pavia, Italy

Site 1
Rome, Italy

Poland
Site 1
Lublin, Poland

Site 4
Tychy, Poland

Site 3
Wroclaw, Poland

Spain
Site 5
Alicante, Spain

Site 1
Badalona, Spain

Site 7
Guadalajara, Spain

Site 6
Madrid, Spain

Site 8
Navarra, Spain

Site 4
Oviedo, Spain

Switzerland
Site 1
Morges, Switzerland

Site 2
Valens, Switzerland

United Kingdom
Site 2
Bristol, United Kingdom

Site 1
Glasgow, United Kingdom

Site 4
London, United Kingdom

Site 5
London, United Kingdom

Site 3
Plymouth, United Kingdom

Germany
Site 8
Leipzig, Germany

Spain
Site 3
Valencia, Spain

United Kingdom
Site 6
Edinburgh, United Kingdom

Site 7
Belfast, United Kingdom

Site 8
Chelmsford, United Kingdom

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	The trial started on 30 September 2009 with enrollment of the first subject and the last follow-up examination took place on 06 July 2010.
Pre-Assignment Details	During the observation period (3 to 7 days in length) subjects recorded their analgesic medication intake and pain intensity. Prior to intake of tapentadol.

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Observation Period

	Tapentadol
Started	208
Completed	176
Not Completed	32
Not eligible to be dosed	20
Not Evaluable due to Non Compliance	12

Titration and Optimal Dose Period

	Tapentadol
Started	176
Completed	140
Not Completed	36

Maintenance Period

	Tapentadol
Started	140
Completed	117
Not Completed	23

Baseline Characteristics

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Baseline Measures

	Tapentadol
Number of Participants	176
Age, Continuous [units: years] Mean (Standard Deviation)	59.7 (11.8)
Gender, Male/Female [units: participants]	
Female	111
Male	65
Region of Enrollment [units: participants]	
France	14
Spain	52
Poland	11
Croatia	0
Austria	26
Germany	46
United Kingdom	12
Switzerland	3
Italy	12
Prior analgesic medication [units: participants]	
Participants pretreated with opioids	88
Participants opioid naive (Step 1 analgesics)	87
Unknown	1

Outcome Measures

1. Primary Outcome Measure:

Measure Title	The Primary Endpoint is Defined as the Change of the Average Pain Intensity Score on an 11-point NRS-3 at Week 6 From Week -1 (Baseline).
Measure Description	For this pain assessment, the participant was to indicate the level of average pain experienced over the previous 3 days on an 11-point Numerical Rating Scale(NRS) where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine". The value indicates the change from the baseline participant assessment on the 0 to 10 scale. A negative value indicates a reduction in pain intensity.
Time Frame	Baseline; End of Week 6 (6 Weeks)
Safety Issue?	No

Analysis Population Description

Intention to treat. Last Observation Carried Forward (LOCF)

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	174
The Primary Endpoint is Defined as the Change of the Average Pain Intensity Score on an 11-point NRS-3 at Week 6 From Week -1 (Baseline). [units: Units on a scale] Mean (Standard Deviation)	-2.8 (2.12)

2. Secondary Outcome Measure:

Measure Title	Patient Global Impression of Change at End of Titration and Optimal Dose Period

Measure Description	In the Patient Global Impression of Change (PGIC) the participant indicates the perceived change over the treatment period. The participant is requested to choose one of seven categories. Scores range from very much improved to very much worse.
Time Frame	Baseline; End of Week 6 (6 Weeks)
Safety Issue?	No

Analysis Population Description
Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	134
Patient Global Impression of Change at End of Titration and Optimal Dose Period [units: participants]	
Very much improved	12
Much improved	55
Minimally improved	49
No change	10
Minimally worse	5
Much worse	2
Very much worse	1

3. Secondary Outcome Measure:

Measure Title	Patient Global Impression of Change at End of the Maintenance Period
Measure Description	In the Patient Global Impression of Change (PGIC) the participant indicates the perceived change over the treatment period. The participant is requested to choose one of seven categories. Scores range from very much improved to very much worse.
Time Frame	Baseline; End of Week 12 (12 weeks)
Safety Issue?	No

Analysis Population Description
Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	89
Patient Global Impression of Change at End of the Maintenance Period [units: participants]	
Very much improved	19
Much improved	42
Minimally improved	23
No change	5
Minimally worse	0
Much worse	0
Very much worse	0

4. Secondary Outcome Measure:

Measure Title	Change in the Health Survey Scores Form (SF-36) at End of Titration and Optimal Dose Period
Measure Description	The Scores Form 36 (SF-36) includes several brief board questions on 8 aspects, (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health) that a participant was asked to score over the last week. A higher score indicates an improvement in health. All domains are scored on a scale from 0 (negative health) to 100 (positive health), with 100 representing the best possible health state. A positive mean value indicates an improvement from baseline.
Time Frame	Baseline; End of Week 6 (6 weeks)
Safety Issue?	No

Analysis Population Description
Intention to treat (ITT)

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	133
Change in the Health Survey Scores Form (SF-36) at End of Titration and Optimal Dose Period [units: Units on a scale] Mean (Standard Deviation)	
Physical Functioning	14.1 (17.23)
Bodily Pain	21.7 (21.39)
General Health	6.3 (16.18)
Vitality	8.0 (20.28)
Social Functioning	10.7 (25.84)

	Tapentadol
Role Emotional	14.8 (43.98)
Mental Health	7.5 (18.22)
Role Physical	25.0 (40.47)

5. Secondary Outcome Measure:

Measure Title	Change in the Health Survey Scores Form (SF-36) at End of Maintenance Period
Measure Description	The Scores Form 36 (SF-36) includes several brief board questions on 8 aspects, (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health) that a participant was asked to score over the last week. A higher score indicates an improvement in health. All domains are scored on a scale from 0 (negative health) to 100 (positive health), with 100 representing the best possible health state. A positive mean value indicates an improvement from baseline.
Time Frame	Baseline; End of Week 12 (12 weeks)
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	89
Change in the Health Survey Scores Form (SF-36) at End of Maintenance Period [units: Units on a scale] Mean (Standard Deviation)	

	Tapentadol
Physical Functioning	15.7 (21.95)
Bodily Pain	24.4 (21.96)
General Health	10.3 (14.95)
Vitality	9.5 (18.43)
Social Functioning	13.2 (27.85)
Role Emotional	18.6 (44.17)
Mental Health	12.0 (18.33)
Role Physical	29.2 (48.30)

6. Secondary Outcome Measure:

Measure Title	painDETECT Assessment at Baseline
Measure Description	The painDETECT questionnaire was used to determine the possibility of the presence of a neuropathic pain component. It is a participant completed questionnaire. A total score is calculated. Participants with a score between 0 and 12 are scored as being "negative" (no neuropathic pain component). Value between 19 and 38 as being "positive" (presence of neuropathic component)". Values from 13 to 18 are scored as being "unclear".
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description
Intention to treat (ITT).

Reporting Groups

	Description
Baseline painDETECT Negative Group	Subgroup of participants with a score between 0 and 12.
Baseline painDETECT Unclear Group	Subgroup of participants with a score between 13 and 18.
Baseline painDETECT Positive Group	Subgroup of participants with a score between 19 and 38.

Measured Values

	Baseline painDETECT Negative Group	Baseline painDETECT Unclear Group	Baseline painDETECT Positive Group
Number of Participants Analyzed	49	41	81
painDETECT Assessment at Baseline [units: units on a scale] Mean (Standard Deviation)	7.1 (3.26)	13.2 (3.36)	21.4 (5.05)

7. Secondary Outcome Measure:

Measure Title	painDETECT Assessment for Participants at End of Titration and Optimal Dose Period
Measure Description	The baseline painDETECT score was reassessed at the end of Week 6. It is a participant completed questionnaire. A total score is calculated. Participants with a score between 0 and 12 are scored as being "negative" (no neuropathic pain component). Value between 19 and 38 as being "positive" (presence of neuropathic component)". Values from 13 to 18 are scored as being "unclear".
Time Frame	End of Week 6
Safety Issue?	No

Analysis Population Description
Intention to treat (ITT).

Reporting Groups

	Description
Baseline painDETECT Negative Group	The subgroup of participants scoring 0-12 at the baseline painDETECT assessment were reassessed at the end of Week 6.
Baseline painDETECT Unclear Group	The subgroup of participants scoring 13-18 at the baseline painDETECT assessment were reassessed at the end of Week 6.
Baseline painDETECT Positive Group	The subgroup of participants scoring 19-38 at the baseline painDETECT assessment were reassessed at the end of Week 6.

Measured Values

	Baseline painDETECT Negative Group	Baseline painDETECT Unclear Group	Baseline painDETECT Positive Group
Number of Participants Analyzed	34	32	64

	Baseline painDETECT Negative Group	Baseline painDETECT Unclear Group	Baseline painDETECT Positive Group
painDETECT Assessment for Participants at End of Titration and Optimal Dose Period [units: units on a scale] Mean (Standard Deviation)	5.5 (3.60)	9.8 (6.21)	14.4 (7.05)

8. Secondary Outcome Measure:

Measure Title	painDETECT Assessment for Participants at End of the Maintenance Period
Measure Description	The baseline painDETECT score was reassessed at the end of Week 12. It is a participant completed questionnaire. A total score is calculated. Participants with a score between 0 and 12 are scored as being "negative" (no neuropathic pain component). Value between 19 and 38 as being "positive" (presence of neuropathic component)". Values from 13 to 18 are scored as being "unclear".
Time Frame	End of Week 12
Safety Issue?	No

Analysis Population Description
Intention to treat (ITT).

Reporting Groups

	Description
Baseline painDETECT Negative Group	The subgroup of participants scoring 0-12 at the baseline painDETECT assessment were reassessed at the end of Week 12.
Baseline painDETECT Unclear Group	The subgroup of participants scoring 13-18 at the baseline painDETECT assessment were reassessed at the end of Week 12.
Baseline painDETECT Positive Group	The subgroup of participants scoring 19-38 at the baseline painDETECT assessment were reassessed at the end of Week 12.

Measured Values

	Baseline painDETECT Negative Group	Baseline painDETECT Unclear Group	Baseline painDETECT Positive Group
Number of Participants Analyzed	23	21	45
painDETECT Assessment for Participants at End of the Maintenance Period [units: units on a scale]	5.7 (4.22)	7.1 (6.13)	11.2 (7.52)

	Baseline painDETECT Negative Group	Baseline painDETECT Unclear Group	Baseline painDETECT Positive Group
Mean (Standard Deviation)			

9. Secondary Outcome Measure:

Measure Title	Neuropathic Pain Symptom Inventory (NPSI) Subscores and Overall Score Assessment at Baseline
Measure Description	Mean score NPSI (Neuropathic Pain Symptom Inventory). The participant rates their symptoms of neuropathic pain. Ten pain questions are answered on an 11-point scale 0 (no pain) to 10 (most intense pain imaginable). Two items related to temporal pain assessed on 5-point scales.
Time Frame	Baseline Visit
Safety Issue?	No

Analysis Population Description
Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	124
Neuropathic Pain Symptom Inventory (NPSI) Subscores and Overall Score Assessment at Baseline [units: units on a scale] Mean (Standard Deviation)	
Sub-score burning pain	0.470 (0.310)
Sub-score pressing pain	0.549 (0.243)
Sub-score paroxysmal pain	0.575 (0.243)

	Tapentadol
Sub-score evoked pain	0.391 (0.263)
Sub-score paresthesia / dysthesia	0.539 (0.273)
Overall score	0.497 (0.180)

10. Secondary Outcome Measure:

Measure Title	Neuropathic Pain Symptom Inventory (NPSI) Subscores and Overall Score at End of Titration and Optimal Dose Period
Measure Description	Mean score NPSI (Neuropathic Pain Symptom Inventory). The participant rates their symptoms of neuropathic pain. Ten pain questions are answered on an 11-point scale 0 (no pain) to 10 (most intense pain imaginable). Two items related to temporal pain assessed on 5-point scales.
Time Frame	End of Week 6
Safety Issue?	No

Analysis Population Description
Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	97
Neuropathic Pain Symptom Inventory (NPSI) Subscores and Overall Score at End of Titration and Optimal Dose Period [units: units on a scale] Mean (Standard Deviation)	
Sub-score burning pain	0.260 (0.281)

	Tapentadol
Sub-score pressing pain	0.316 (0.257)
Sub-score paroxysmal pain	0.293 (0.258)
Sub-score evoked pain	0.230 (0.221)
Sub-score paresthesia / dysthesia	0.303 (0.2722)
Overall score	0.278 (0.204)

11. Secondary Outcome Measure:

Measure Title	Neuropathic Pain Symptom Inventory (NPSI) Subscores and Overall Score Assessment at End of the Maintenance Period
Measure Description	Mean score NPSI (Neuropathic Pain Symptom Inventory). The participant rates their symptoms of neuropathic pain. Ten pain questions are answered on an 11-point scale 0 (no pain) to 10 (most intense pain imaginable). Two items related to temporal pain assessed on 5-point scales.
Time Frame	End of Week 12
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	66

	Tapentadol
Neuropathic Pain Symptom Inventory (NPSI) Subscores and Overall Score Assessment at End of the Maintenance Period [units: units on a scale] Mean (Standard Deviation)	
Sub-score burning pain	0.180 (0.237)
Sub-score pressing pain	0.235 (0.218)
Sub-score paroxysmal pain	0.211 (0.225)
Sub-score evoked pain	0.175 (0.188)
Sub-score paresthesia / dysthesia	0.231 (0.270)
Overall score	0.206 (0.198)

12. Secondary Outcome Measure:

Measure Title	Change in Neuropathic Pain Symptom Inventory (NPSI) Final Score Assessment at End of Titration and Optimal Dose Period
Measure Description	Change in mean score NPSI, questionnaire evaluates symptoms of neuropathic pain. Ten pain descriptors questions are answered on an 11-point scale 0 (no pain)-10 (most intense pain imaginable). The NPSI derives a total intensity score calculated from the subscores. A negative value indicates improvement in neuropathic symptoms.
Time Frame	Baseline; End of Week 6 (6 Weeks)
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT), Last Observation Carried Forward (LOCF).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	95
Change in Neuropathic Pain Symptom Inventory (NPSI) Final Score Assessment at End of Titration and Optimal Dose Period [units: Units on a scale] Mean (Standard Deviation)	-0.224 (0.213)

13. Secondary Outcome Measure:

Measure Title	Change in Neuropathic Pain Symptom Inventory (NPSI) Final Score Assessment at End of the Maintenance Period
Measure Description	Change in mean score NPSI, questionnaire evaluates symptoms of neuropathic pain. Ten pain descriptors questions are answered on an 11-point scale 0 (no pain)-10 (most intense pain imaginable). The NPSI derives a total intensity score calculated from the subscores. A negative value indicates improvement in neuropathic symptoms.
Time Frame	Baseline; End of Week 12 (12 Weeks)
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT), Last Observation Carried Forward (LOCF).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	65
Change in Neuropathic Pain Symptom Inventory (NPSI) Final Score Assessment at End of the Maintenance Period	-0.296 (0.228)

	Tapentadol
[units: units on a scale] Mean (Standard Deviation)	

14. Secondary Outcome Measure:

Measure Title	EuroQol-5 (EQ-5D) Health Status Index Outcome Over Time at End of Titration and Optimal Dose Period.
Measure Description	The participant scored the EuroQol-5. This is a five dimensional health state classification. Each dimension is assessed on a 3-point ordinal scale (1=no problems, 2=some problems, 3=extreme problems). The responses to the five EQ-5D dimensions were scored using a utility-weighted algorithm to derive an EQ-5D health status index score between 0 to 1, with 1.00 indicating "full health" and 0 representing dead. The positive values indicate that during the study the health status improved.
Time Frame	Baseline; End of Week 6 (6 weeks)
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT). painDETECT negative subpopulation - 35 participants. Unclear and positive painDETECT subpopulation - 98 participants.

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	133
EuroQol-5 (EQ-5D) Health Status Index Outcome Over Time at End of Titration and Optimal Dose Period. [units: Units on a scale] Mean (Standard Deviation)	
All participants	0.244 (0.315)

	Tapentadol
Participants painDETECT negative	0.229 (0.321)
Participant painDETECT unclear or positive	0.249 (0.315)

15. Secondary Outcome Measure:

Measure Title	Change in Health Related Quality of Life: EuroQol-5D Health State Visual Analog Scale (VAS)at End of Titration and Optimal Dose Period.
Measure Description	EuroQoL-5D Health State Visual Analog Scale (VAS) is a participant rated questionnaire to assess health-related quality of life in terms of a single index value. The VAS component rates current health state on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state); higher scores indicate a better health state. The values indicated represent the change from the baseline, a positive value indicates an improvement.
Time Frame	Baseline; End of Week 6 (6 weeks)
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT). painDETECT negative subpopulation - 34 participants. Unclear and positive painDETECT subpopulation - 97 participants.

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	131
Change in Health Related Quality of Life: EuroQol-5D Health State Visual Analog Scale (VAS)at End of Titration and Optimal Dose Period. [units: Units on a scale] Mean (Standard Deviation)	

	Tapentadol
All participants	12.2 (25.08)
Participants painDETECT negative	7.6 (19.74)
Participant painDETECT unclear or positive	13.8 (26.61)

16. Secondary Outcome Measure:

Measure Title	EuroQol-5 (EQ-5D) Health Status Index Outcome Over Time at End of Maintenance Period
Measure Description	The participant scored the EuroQol-5. This is a five dimensional health state classification. Each dimension is assessed on a 3-point ordinal scale (1=no problems, 2=some problems, 3=extreme problems). The responses to the five EQ-5D dimensions were scored using a utility-weighted algorithm to derive an EQ-5D health status index score between 0 to 1, with 1.00 indicating "full health" and 0 representing dead. The positive values indicate that during the study the health status improved.
Time Frame	Baseline; End of Week 12 (12 weeks)
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT). Unclear and positive painDETECT subpopulation - 66 participants. painDETECT negative subpopulation - 23 participants.

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	89
EuroQol-5 (EQ-5D) Health Status Index Outcome Over Time at End of Maintenance Period [units: units on a scale] Mean (Standard Deviation)	

	Tapentadol
All participants	0.282 (0.297)
Participants painDETECT negative	0.182 (0.252)
Participants painDETECT unclear or positive	0.316 (0.306)

17. Secondary Outcome Measure:

Measure Title	Change in Health Related Quality of Life: EuroQol-5D Health State Visual Analog Scale (VAS) at End of Maintenance Period
Measure Description	EuroQoL-5D Health State Visual Analog Scale (VAS) is a participant rated questionnaire to assess health-related quality of life in terms of a single index value. The VAS component rates current health state on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state); higher scores indicate a better health state. The values indicated represent the change from the baseline, a positive value indicates an improvement.
Time Frame	Baseline; End of Week 12 (12 weeks)
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT). painDETECT negative subpopulation - 23 participants. Unclear and positive painDETECT subpopulation - 66 participants.

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	89
Change in Health Related Quality of Life: EuroQol-5D Health State Visual Analog Scale (VAS) at End of Maintenance Period [units: Units on a scale]	

	Tapentadol
Mean (Standard Deviation)	
All participants	20.0 (27.27)
Participants painDETECT negative	14.7 (26.68)
Participant painDETECT unclear or positive	21.8 (27.44)

18. Secondary Outcome Measure:

Measure Title	Clinical Global Impression of Change (All Participants) at End of Titration and Optimal Dose Period
Measure Description	In the Clinical Global Impression of Change (CGIC) the clinician indicates the perceived change over the treatment period. The clinician is requested to choose one of seven categories. Scores range from very much improved to very much worse.
Time Frame	Baseline; End of Week 6 (6 weeks)
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	134
Clinical Global Impression of Change (All Participants) at End of Titration and Optimal Dose Period [units: participants]	
Very much improved	17

	Tapentadol
Much improved	53
Minimally improved	49
No change	11
Minimally worse	2
Much worse	1
Very much worse	1

19. Secondary Outcome Measure:

Measure Title	Clinical Global Impression of Change (All Participants) at End of Maintenance Period
Measure Description	In the Clinical Global Impression of Change (CGIC) the clinician indicates the perceived change over the treatment period. The clinician is requested to choose one of seven categories. Scores range from very much improved to very much worse.
Time Frame	Baseline; End of Week 12 (12 weeks)
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	89

	Tapentadol
Clinical Global Impression of Change (All Participants) at End of Maintenance Period [units: participants]	
Very much improved	17
Much improved	45
Minimally improved	22
No change	5

20. Secondary Outcome Measure:

Measure Title	Hospital Anxiety Depression Scale: Anxiety Score at Baseline
Measure Description	Anxiety Scale - 7 items scored for each individual question from 0 = best and 3 = worst. HADS is a self-assessment scale for the symptom severity of anxiety disorders and depression. It comprises of 14 items. Seven statements describe anxiety. Each answer is scored on a four-point scale (0-3). All seven answers are summed to a total score with a maximum score of 21 points. A negative value indicates that there has been an improvement.
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

Negative painDETECT subpopulation - 49 participants Unclear and positive painDETECT subpopulation - 124 participants Intention to Treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	173
Hospital Anxiety Depression Scale: Anxiety Score at Baseline [units: units on a scale] Mean (Standard Deviation)	
All participants	7.8 (4.32)
Negative painDETECT participants	6.2 (4.10)
Unclear and positive painDETECT participants	8.4 (4.26)

21. Secondary Outcome Measure:

Measure Title	Hospital Anxiety Depression Scale: Change in Anxiety Score at End of Titration and Optimal Dose Period
Measure Description	Anxiety Scale - 7 items scored for each individual question from 0 = best and 3 = worst. HADS is a self-assessment scale for the symptom severity of anxiety disorders and depression. It comprises of 14 items. Seven statements describe anxiety. Each answer is scored on a four-point scale (0-3). All seven answers are summed to a total score with a maximum score of 21 points. A negative value indicates that there has been an improvement.
Time Frame	Baseline; End of Week 6 (6 weeks)
Safety Issue?	No

Analysis Population Description

Negative painDETECT subpopulation - 34 participants Unclear and positive painDETECT subpopulation - 94 participants Intention to Treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	128
Hospital Anxiety Depression Scale: Change in Anxiety Score at End of Titration and Optimal Dose Period [units: units on a scale] Mean (Standard Deviation)	
All participants	-1.2 (3.36)
Negative painDETECT participants	-0.3 (2.93)
Unclear and positive painDETECT participants	-1.5 (3.47)

22. Secondary Outcome Measure:

Measure Title	Hospital Anxiety Depression Scale: Change in Anxiety Score at End of Maintenance Period
Measure Description	Anxiety Scale - 7 items scored for each individual question from 0 = best and 3 = worst. HADS is a self-assessment scale for the symptom severity of anxiety disorders and depression. It comprises of 14 items. Seven statements describe anxiety. Each answer is scored on a four-point scale (0-3). All seven answers are summed to a total score with a maximum score of 21 points. A negative value indicates that there has been an improvement.
Time Frame	Baseline; End of Week 12 (12 Weeks)
Safety Issue?	No

Analysis Population Description

Negative painDETECT subpopulation - 23 participants Unclear and positive painDETECT subpopulation - 66 participants Intention to Treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	89
Hospital Anxiety Depression Scale: Change in Anxiety Score at End of Maintenance Period [units: units on a scale] Mean (Standard Deviation)	
All participants	-2.1 (3.67)
Negative painDETECT participants	-0.8 (2.82)
Unclear and positive painDETECT participants	-2.5 (3.85)

23. Secondary Outcome Measure:

Measure Title	Hospital Anxiety Depression Scale: Depression Score at Baseline
Measure Description	Depression Scale - 7 items scored for each individual question from 0 = best and 3 = worst. HADS is a self-assessment scale for the symptom severity of anxiety disorders and depression. It comprises of 14 items. Seven statements describe anxiety. Each answer is scored on a four-point scale (0-3). All seven answers are summed to a total score with a maximum score of 21 points. A negative value indicates that there has been an improvement.
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

Negative painDETECT subpopulation - 49 participants Unclear and positive painDETECT subpopulation - 124 participants Intention to Treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	173
Hospital Anxiety Depression Scale: Depression Score at Baseline [units: units on a scale] Mean (Standard Deviation)	
All participants	7.9 (4.27)
Negative painDETECT participants	6.5 (3.96)
Unclear and positive painDETECT participants	8.5 (4.27)

24. Secondary Outcome Measure:

Measure Title	Hospital Anxiety Depression Scale: Change in Depression Score at End of Titration and Optimal Dose Period.
Measure Description	Depression Scale - 7 items scored for each individual question from 0 = best and 3 = worst. HADS is a self-assessment scale for the symptom severity of anxiety disorders and depression. It comprises of 14 items. Seven statements describe depression. Each answer is scored on a four-point scale (0-3). All seven answers are summed to a total score with a maximum score of 21 points. A negative value indicates that there has been an improvement.
Time Frame	Baseline; End of Week 6 (6 weeks)
Safety Issue?	No

Analysis Population Description

Negative painDETECT subpopulation - 34 participants Unclear or positive painDETEC subpopulation - 94 participants Intention to Treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	128
Hospital Anxiety Depression Scale: Change in Depression Score at End of Titration and Optimal Dose Period. [units: units on a scale] Mean (Standard Deviation)	
All participants	-1.2 (3.40)
Negative painDETECT participants	-1.0 (3.15)
Unclear and positive painDETECT participants	-1.3 (3.50)

25. Secondary Outcome Measure:

Measure Title	Hospital Anxiety Depression Scale: Change in Depression Score at End of Maintenance Period
Measure Description	Depression Scale - 7 items scored for each individual question from 0 = best and 3 = worst. HADS is a self-assessment scale for the symptom severity of anxiety disorders and depression. It comprises of 14 items. Seven statements describe depression. Each answer is scored on a four-point scale (0-3). All seven answers are summed to a total score with a maximum score of 21 points. A negative value indicates that there has been an improvement.
Time Frame	Baseline; End of Week 12 (12 Weeks)
Safety Issue?	No

Analysis Population Description

Negative painDETECT subpopulation - 23 participants Unclear and positive painDETECT subpopulation - 66 participants.

Intention to Treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	89
Hospital Anxiety Depression Scale: Change in Depression Score at End of Maintenance Period [units: units on a scale] Mean (Standard Deviation)	
All participants	-1.6 (3.24)
Negative painDETECT participants	-0.5 (2.86)
Unclear and positive painDETECT participants	-2.0 (3.30)

26. Secondary Outcome Measure:

Measure Title	Final Stable Tapentadol PR Dose in Opioid Naive Participants at End of Titration and Optimal Dose Period.
Measure Description	Tapentadol hydrochloride PR dose after 5 weeks of titration which was to be kept stable during the remained of the trial.
Time Frame	Week 6
Safety Issue?	No

Analysis Population Description

Negative painDETECT subpopulation - 22 participants Unclear painDETECT subpopulation - 15 participants Positive painDETECT subpopulation - 22 participants Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	59
Final Stable Tapentadol PR Dose in Opioid Naive Participants at End of Titration and Optimal Dose Period. [units: milligrams (mg)] Mean (Standard Deviation)	
Negative painDETECT participants	336.4 (132.90)
Unclear painDETECT participants	293.3 (103.28)
Positive painDETECT participants	268.2 (132.33)

27. Secondary Outcome Measure:

Measure Title	Participant's Satisfaction With Previous Analgesic Treatment at Baseline
Measure Description	Participants were requested to rate their previous analgesic medication on a 5-point scale. Previous analgesic medication was rated as excellent, very good, good, fair and poor.
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	175
Participant's Satisfaction With Previous Analgesic Treatment at Baseline [units: participants]	
Good	2
Fair	98
Poor	75

28. Secondary Outcome Measure:

Measure Title	Participant's Satisfaction With New Analgesic Treatment, i.e Tapentadol, at the End of Titration and Optimal Dose Period.
Measure Description	Participants were requested to rate their tapentadol (new) analgesic medication on a 5-point scale. The medication was rated as excellent, very good, good, fair and poor.
Time Frame	End of Week 6
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	134
Participant's Satisfaction With New Analgesic Treatment, i.e Tapentadol, at the End of Titration and Optimal Dose Period. [units: participants]	
Excellent	12
Very Good	29
Good	64
Fair	22
Poor	7

29. Secondary Outcome Measure:

Measure Title	Participant's Satisfaction With New Analgesic Treatment, i.e Tapentadol, in the Maintenance Period.
Measure Description	Participants were requested to rate their tapentadol (new) analgesic medication on a 5-point scale. The medication was rated as excellent, very good, good, fair and poor.
Time Frame	End of Week 8
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	122
Participant's Satisfaction With New Analgesic Treatment, i.e Tapentadol, in the Maintenance Period. [units: participants]	
Excellent	14
Very Good	30
Good	58
Fair	17
Poor	3

30. Secondary Outcome Measure:

Measure Title	Participant's Satisfaction With New Analgesic Treatment, i.e Tapentadol, at End of the Maintenance Period.
Measure Description	Participants were requested to rate their tapentadol (new) analgesic medication on a 5-point scale. The medication was rated as excellent, very good, good, fair and poor.
Time Frame	End of Week 12
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT).

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	89
Participant's Satisfaction With New Analgesic Treatment, i.e Tapentadol, at End of the Maintenance Period. [units: participants]	
Excellent	10
Very Good	38
Good	28
Fair	11
Poor	2

31. Secondary Outcome Measure:

Measure Title	Baseline NRS-3 Pain Intensity in Participants With No Prior Opioid Treatment, at Baseline.
Measure Description	For this pain assessment, the participant was to indicate the level of average pain experienced over the previous 3 days on an 11-point Numerical Rating Scale(NRS) where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine".
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT). Negative painDETECT subpopulation - 31 participants. Unclear and positive painDETECT subpopulation - 56 participants

Reporting Groups

	Description
Tapentadol	Baseline(week -1) NRS-3 pain intensity values in PainDetect specific subgroup of participants that entered the titration and optimal dose period. All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	87
Baseline NRS-3 Pain Intensity in Participants With No Prior Opioid Treatment, at Baseline. [units: Units on a scale] Mean (Standard Deviation)	
Negative painDETECT participants	7.3 (0.78)
Unclear and positive painDETECT participants	7.4 (1.00)

32. Secondary Outcome Measure:

Measure Title	NRS-3 Pain Intensity in Participants With No Prior Opioid Treatment at the End of the Titration and Optimal Dose Period.
Measure Description	For this pain assessment, the participant was to indicate the level of average pain experienced over the previous 3 days on an 11-point Numerical Rating Scale(NRS) where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine".
Time Frame	End of Week 6
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT). Negative painDETECT subpopulation - 22 participants. Unclear and positive painDETECT subpopulation - 37 participants

Reporting Groups

	Description
Tapentadol	NRS-3 pain intensity values at End of Week 6 in PainDetect specific subgroup of participants that entered the titration and optimal dose period. All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	59
NRS-3 Pain Intensity in Participants With No Prior Opioid Treatment at the End of the Titration and Optimal Dose Period. [units: Units on a scale] Mean (Standard Deviation)	
Negative painDETECT participants	4.0 (1.77)
Unclear and positive painDETECT participants	4.1 (1.86)

33. Secondary Outcome Measure:

Measure Title	NRS-3 Pain Intensity in Participants With No Prior Opioid Treatment at the End of the Maintenance Period.
Measure Description	For this pain assessment, the participant was to indicate the level of average pain experienced over the previous 3 days on an 11-point Numerical Rating Scale(NRS) where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine".
Time Frame	End of Week 12
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT). Negative painDETECT subpopulation - 15 participants. Unclear and positive painDETECT subpopulation - 24 participants

Reporting Groups

	Description
Tapentadol	NRS-3 pain intensity values at End of Week 12 in PainDetect specific subgroup of participants that entered the maintenance period. All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	39
NRS-3 Pain Intensity in Participants With No Prior Opioid Treatment at the End of the Maintenance Period. [units: Units on a scale] Mean (Standard Deviation)	
Negative painDETECT participants	3.1 (1.81)
Unclear and positive painDETECT participants	3.4 (2.32)

34. Secondary Outcome Measure:

Measure Title	Baseline NRS-3 Pain Intensity in Participants With Prior Opioid Treatment, at Baseline.
Measure Description	For this pain assessment, the participant was to indicate the level of average pain experienced over the previous 3 days on an 11-point Numerical Rating Scale(NRS) where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine".
Time Frame	Baseline
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT). Negative painDETECT subpopulation - 18 participants. Unclear and positive painDETECT subpopulation - 70 participants

Reporting Groups

	Description
Tapentadol	Baseline(week -1) NRS-3 pain intensity values in PainDetect specific subgroup of participants, with prior opioid treatment, that entered the titration and optimal dose period.

Measured Values

	Tapentadol
Number of Participants Analyzed	88
Baseline NRS-3 Pain Intensity in Participants With Prior Opioid Treatment, at Baseline. [units: Units on a scale] Mean (Standard Deviation)	
Negative painDETECT participants	6.7 (0.96)
Unclear and positive painDETECT participants	7.6 (1.07)

35. Secondary Outcome Measure:

Measure Title	NRS-3 Pain Intensity Assessment in Participants With Prior Opioid Treatment at the End of the Titration and Optimal Dose Period.
Measure Description	For this pain assessment, the participant was to indicate the level of average pain experienced over the previous 3 days on an 11-point Numerical Rating Scale(NRS) where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine".
Time Frame	End of Week 6
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT). Negative painDETECT subpopulation - 13 participants. Unclear and positive painDETECT subpopulation - 62 participants

Reporting Groups

	Description
Tapentadol	NRS-3 pain intensity values at end of Week 6 in painDetect specific subgroup of participants, with prior opioid treatment, that entered the titration and optimal dose period. All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	75
NRS-3 Pain Intensity Assessment in Participants With Prior Opioid Treatment at the End of the Titration and Optimal Dose Period. [units: Units on a scale] Mean (Standard Deviation)	
Negative painDETECT participants	4.2 (1.96)
Unclear and positive painDETECT participants	4.4 (2.26)

36. Secondary Outcome Measure:

Measure Title	NRS-3 Pain Intensity Assessment in Participants With Prior Opioid Treatment at the End of the Maintenance Period.
Measure Description	For this pain assessment, the participant was to indicate the level of average pain experienced over the previous 3 days on an 11-point Numerical Rating Scale(NRS) where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine".
Time Frame	End of Week 12
Safety Issue?	No

Analysis Population Description

Intention to treat (ITT). Negative painDETECT subpopulation - 8 participants. Unclear and positive painDETECT subpopulation - 42 participants

Reporting Groups

	Description
Tapentadol	NRS-3 pain intensity values at End of Week 12 in painDetect specific subgroup of participants, with prior opioid treatment, that entered the maintenance period. All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Measured Values

	Tapentadol
Number of Participants Analyzed	50
NRS-3 Pain Intensity Assessment in Participants With Prior Opioid Treatment at the End of the Maintenance Period. [units: Units on a scale] Mean (Standard Deviation)	
Negative painDETECT participants	3.4 (1.92)
Unclear and positive painDETECT participants	3.2 (1.94)

Reported Adverse Events

Time Frame	12 weeks
Additional Description	The total daily dose of tapentadol hydrochloride PR ranged from 50 mg to 500 mg.

Reporting Groups

	Description
Tapentadol	All participants started with 50 mg tapentadol hydrochloride PR (twice daily). The dose of tapentadol hydrochloride PR was adjusted to a level that provided adequate analgesia (upwards or downwards on a weekly basis as needed). After 5 weeks the doses of tapentadol hydrochloride was kept stable. Participants were permitted a maximum dose of 250 mg twice a day (500 mg total daily dose). Tapentadol hydrochloride IR 50 mg (no more than twice daily; at least 4 hours apart) was considered as medication for acute pain episodes, however participants were not permitted to dose tapentadol hydrochloride IR once 500 mg tapentadol hydrochloride PR dose was reached.

Serious Adverse Events

	Tapentadol
	Affected/At Risk (%)
Total	7/176 (3.98%)
Hepatobiliary disorders	
Cholecystitis acute [A] *	1/176 (0.57%)
Infections and infestations	
Sepsis [A] *	1/176 (0.57%)
Investigations	
Blood insulin abnormal [A] *	1/176 (0.57%)
Metabolism and nutrition disorders	
Type 2 diabetes mellitus [A] *	1/176 (0.57%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Renal cell carcinoma [A] *	1/176 (0.57%)
Psychiatric disorders	
Confusional state [A] *	1/176 (0.57%)
Renal and urinary disorders	
Renal colic [A] *	1/176 (0.57%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA 13.0

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Tapentadol
	Affected/At Risk (%)
Total	148/176 (84.09%)
Gastrointestinal disorders	
Abdominal upper pain [A] *	9/176 (5.11%)
Constipation [A] *	20/176 (11.36%)
Diarrhoea [A] *	20/176 (11.36%)
Dry mouth [A] *	27/176 (15.34%)
Nausea [A] *	37/176 (21.02%)
Vomiting [A] *	11/176 (6.25%)
General disorders	
Fatigue [A] *	22/176 (12.5%)
Infections and infestations	
Nasopharyngitis [A] *	20/176 (11.36%)
Nervous system disorders	
Dizziness [A] *	31/176 (17.61%)
Headache [A] *	29/176 (16.48%)
Somnolence [A] *	18/176 (10.23%)
Skin and subcutaneous tissue disorders	
Hyperhidrosis [A] *	9/176 (5.11%)
Pruritus [A] *	9/176 (5.11%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA 13.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Grünenthal reserves the right to review any publication pertaining to the trial before it is submitted for publication. Neither party has the right to prohibit publication unless publication can be shown to affect possible patent rights.

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