



Clinical trial results:

Efficacy and safety of lidocaine 5% medicated plaster in localized chronic post-operative neuropathic pain

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2012-000347-28 |
| Trial protocol | BE AT ES IT DK FR GB |
| Global end of trial date | 21 June 2016 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 30 June 2017 |
| First version publication date | 30 June 2017 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | KF10004-10 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-----------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | U1111-1143-2130 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Grünenthal GmbH |
| Sponsor organisation address | Zieglerstr. 6, Aachen, Germany, 52078 |
| Public contact | GRT Trial Information Desk, Grünenthal GmbH, +49 2415693223, Clinical-Trials@grunenthal.com |
| Scientific contact | GRT Trial Information Desk, Grünenthal GmbH, +49 2415693223, Clinical-Trials@grunenthal.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 | 11 May 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 June 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 June 2016 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the superiority of the analgesic efficacy of lidocaine 5% medicated plaster in comparison to placebo in subjects with moderate to severe localized chronic post-operative neuropathic pain (PoNP).

Protection of trial subjects:

The trial was conducted according to Good Clinical Practice guidelines, the applicable local laws, and in accordance with the ethical principles that have their origins in the Declaration of Helsinki.

The competent authorities approved the trial as required by national regulations.

Regulatory authorities were notified of the trial and amendments as required by national regulations.

Background therapy:

Allowed concomitant medications and therapies were:

Stable systemic medication (used on 5 days or more weekly) for the treatment of PoNP, e.g., antidepressants or anticonvulsants. The treatment regimen (dosage and frequency of administration) must have been stable for at least 1 month before Visit 1 (Enrollment Visit) and remained unchanged until the end of the Double-blind Treatment Period (Visit 5 [End-of-treatment Visit]) or the Discontinuation Visit.

Stable systemic medication (used on 5 days or more weekly) for any other condition that may have also affected the intensity of PoNP or perception of pain in general (e.g., antidepressants, anticonvulsants, benzodiazepines). The treatment regimen (dosage and frequency of administration) must have been stable for at least 1 month before Visit 1 and remained unchanged from Visit 1 until the end of the Double-blind Treatment Period (Visit 5 or the Discontinuation Visit).

For the treatment of acute painful conditions other than PoNP (e.g., headache) for the duration of the trial from Visit 1 until Visit 5 or the Discontinuation Visit:

– Paracetamol (not more than 3 g per day for a maximum of 3 consecutive days). The total amount was limited to 15 g per 28 days unless used for stable treatment.

OR

– Ibuprofen (not more than 1200 mg daily for a maximum of 3 consecutive days). The total amount was limited to 6 g per 28 days unless used for stable treatment.

Treatment for any other condition that did not affect the intensity of PoNP, perception of pain in general, or that did not cause PoNP.

Evidence for comparator:

N/A

| | |
|---|-----------------|
| Actual start date of recruitment | 23 October 2012 |
| 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 | Spain: 18 |
|--------------------------------------|-----------|

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 20 |
| Country: Number of subjects enrolled | Austria: 72 |
| Country: Number of subjects enrolled | Belgium: 42 |
| Country: Number of subjects enrolled | Denmark: 41 |
| Country: Number of subjects enrolled | France: 73 |
| Country: Number of subjects enrolled | Italy: 25 |
| Country: Number of subjects enrolled | Brazil: 68 |
| Worldwide total number of subjects | 359 |
| EEA total number of subjects | 291 |

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) | 290 |
| From 65 to 84 years | 68 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

First subject signed the informed consent on the 23 October 2012 and the last subject completed the trial on the 21 June 2016.

Pre-assignment

Screening details:

A total of 444 subjects were enrolled and signed the informed consent in 42 active sites. 363 of these subjects were allocated to study drug (investigational medicinal product = IMP) and 359 subjects received IMP (180 subjects in the placebo arm, and 179 in the lidocaine arm).

Pre-assignment period milestones

| | |
|------------------------------|--------------------|
| Number of subjects started | 444 ^[1] |
| Number of subjects completed | 359 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|--|
| Reason: Number of subjects | Missing: 4 |
| Reason: Number of subjects | no IMP intake: 4 |
| Reason: Number of subjects | Inclusion criteria not met/exclusion criterion met: 64 |
| Reason: Number of subjects | Consent withdrawn by subject: 9 |
| Reason: Number of subjects | Other reason: 4 |

Notes:

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

Justification: The number of subjects reported to have started the pre-assignment period reflects all subjects who signed an informed consent.

The worldwide number of enrolled subjects is based on the number of subjects allocated to treatment who applied any amount of IMP.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Blinding implementation details:

Subjects have been randomized to receive either lidocaine 5% medicated plasters or placebo plasters. The size of the randomization blocks has not been disclosed to the investigator or any personnel involved in the conduct of the trial. The IMP has been packaged and labeled for each trial medication kit in a blinded fashion on the basis of the randomization schedule. The placebo plaster has been visually indistinguishable from the lidocaine 5% medicated plaster.

Arms

| | |
|------------------------------|--------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Lidocaine 5% medicated plaster |

Arm description:

This arm comprises all subjects allocated to lidocaine 5% medicated plaster who applied any amount of IMP and had at least 1 post-baseline 24-hour average daily pain intensity assessment on the 11-point Numeric rating scale (NRS).

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--------------------------------|
| Investigational medicinal product name | Lidocaine 5% medicated plaster |
| Investigational medicinal product code | GRT10004 |
| Other name | |
| Pharmaceutical forms | Medicated plaster |
| Routes of administration | Topical use |

Dosage and administration details:

Lidocaine 5% medicated plasters were to be applied once daily for no longer than 12 hours within 24 hours with a plaster-free period of at least 12 hours between plaster applications.

Depending on the size of the painful area, up to 3 lidocaine 5% medicated plasters could have been applied simultaneously on the painful skin.

| | |
|------------------|------------------|
| Arm title | Matching Placebo |
|------------------|------------------|

Arm description:

This arm comprises all subjects allocated to placebo plaster who applied any amount of IMP and had at least 1 post-baseline 24-hour average daily pain intensity assessment on the 11-point Numeric rating scale (NRS).

| | |
|--|-------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Medicated plaster |
| Routes of administration | Topical use |

Dosage and administration details:

Placebo plasters were to be applied once daily for no longer than 12 hours within 24 hours with a plaster-free period of at least 12 hours between plaster applications.

Depending on the size of the painful area, up to 3 placebo plasters could have been applied simultaneously on the painful skin.

| Number of subjects in period 1 | Lidocaine 5% medicated plaster | Matching Placebo |
|---------------------------------------|--------------------------------|------------------|
| Started | 179 | 180 |
| Completed | 147 | 147 |
| Not completed | 32 | 33 |
| Consent withdrawn by subject | 3 | 2 |
| Adverse event, non-fatal | 7 | 7 |
| Other reason | 4 | 4 |
| Lost to follow-up | - | 1 |
| Lack of efficacy | 16 | 17 |
| Protocol deviation | 2 | 2 |

Baseline characteristics

Reporting groups

| | |
|--|--------------------------------|
| Reporting group title | Lidocaine 5% medicated plaster |
| Reporting group description: | |
| This arm comprises all subjects allocated to lidocaine 5% medicated plaster who applied any amount of IMP and had at least 1 post-baseline 24-hour average daily pain intensity assessment on the 11-point Numeric rating scale (NRS). | |
| Reporting group title | Matching Placebo |
| Reporting group description: | |
| This arm comprises all subjects allocated to placebo plaster who applied any amount of IMP and had at least 1 post-baseline 24-hour average daily pain intensity assessment on the 11-point Numeric rating scale (NRS). | |

| Reporting group values | Lidocaine 5% medicated plaster | Matching Placebo | Total |
|---|--------------------------------|------------------|-------|
| Number of subjects | 179 | 180 | 359 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 145 | 145 | 290 |
| From 65-84 years | 33 | 35 | 68 |
| 85 years and over | 1 | 0 | 1 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 51.7 | 52.6 | |
| standard deviation | ± 14.2 | ± 13.5 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 117 | 114 | 231 |
| Male | 62 | 66 | 128 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 46 | 42 | 88 |
| Not Hispanic or Latino | 121 | 117 | 238 |
| Not Collected | 12 | 21 | 33 |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 2 | 2 | 4 |
| Asian | 0 | 3 | 3 |
| Black | 4 | 4 | 8 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| White | 164 | 165 | 329 |
| Not Collected | 2 | 2 | 4 |
| Other | 7 | 4 | 11 |
| Height | | | |
| Units: meter | | | |
| arithmetic mean | 1.676 | 1.679 | |
| standard deviation | ± 0.093 | ± 0.093 | - |
| Weight | | | |
| Units: kilogram(s) | | | |

| | | | |
|---------------------------------|---------|---------|---|
| arithmetic mean | 78.17 | 80.14 | |
| standard deviation | ± 16.26 | ± 17.25 | - |
| Body Mass Index (BMI) | | | |
| Units: kilogram(s)/square meter | | | |
| arithmetic mean | 27.81 | 28.45 | |
| standard deviation | ± 5.28 | ± 5.82 | - |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Lidocaine 5% medicated plaster |
| Reporting group description: This arm comprises all subjects allocated to lidocaine 5% medicated plaster who applied any amount of IMP and had at least 1 post-baseline 24-hour average daily pain intensity assessment on the 11-point Numeric rating scale (NRS). | |
| Reporting group title | Matching Placebo |
| Reporting group description: This arm comprises all subjects allocated to placebo plaster who applied any amount of IMP and had at least 1 post-baseline 24-hour average daily pain intensity assessment on the 11-point Numeric rating scale (NRS). | |
| Subject analysis set title | Add-on subjects_Lidocaine 5% medicated plaster |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: This arm comprises all subjects with stable medication for the treatment of PoNP allocated to lidocaine 5% medicated plaster who applied any amount of IMP and had at least 1 post-baseline 24-hour average daily pain intensity assessment on the 11-point Numeric rating scale (NRS). | |
| Subject analysis set title | Add-on subjects_ Matching Placebo |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: This arm comprises all subjects with stable medication for the treatment of PoNP allocated to placebo plaster who applied any amount of IMP and had at least 1 post-baseline 24-hour average daily pain intensity assessment on the 11-point Numeric rating scale (NRS). | |
| Subject analysis set title | Plaster only subjects_Lidocaine 5% medicated plaster |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: This arm comprises all subjects without any additional medication for the treatment of PoNP allocated to lidocaine 5% medicated plaster who applied any amount of IMP and had at least 1 post-baseline 24-hour average daily pain intensity assessment on the 11-point Numeric rating scale (NRS). | |
| Subject analysis set title | Plaster only subjects_Matching Placebo |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: This arm comprises all subjects without any additional medication for the treatment of PoNP allocated to placebo plaster who applied any amount of IMP and had at least 1 post-baseline 24-hour average daily pain intensity assessment on the 11-point Numeric rating scale (NRS). | |

Primary: Change of the 24-hours average pain intensity from baseline to week 12

| | |
|---|--|
| End point title | Change of the 24-hours average pain intensity from baseline to week 12 |
| End point description: The primary efficacy endpoint was the change from baseline of the recorded average pain intensity values during the last 24 hours, averaged over the 7 days of Week 12 of the Double-blind Treatment Period. The 24-hours pain intensity has been assessed once daily before plaster removal using an 11-point numeric rating scale where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine". The baseline value was defined as the calculated mean of the average pain values during the last 24 hours for the last 7 days of the Enrollment Period. A reduction in pain intensity results in negative values. Missing weekly average pain values have been imputed using the multiple imputation (MI) method. | |
| End point type | Primary |
| End point timeframe: Week 12 | |

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|-------------------------------------|--------------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[1] | 180 ^[2] | | |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -1.7 (± 0.16) | -1.47 (± 0.16) | | |

Notes:

[1] - Full Analysis Set using Multiple Imputation Method

[2] - Full Analysis Set using Multiple Imputation method

Statistical analyses

| Statistical analysis title | ANCOVA using Multiple imputation method (MI) |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

An analysis of covariance (ANCOVA) was performed including treatment and concomitant treatment status as factors, and the baseline pain intensity as a covariate using change from baseline on an 11-point NRS as dependent variable. Treatment effects was estimated based on least-squares means (LSmeans) of the difference between Lidocaine Plaster Arm and Placebo Arm and presented together with the corresponding 95% confidence interval (CI) and one-sided p-value for the treatment comparison.

| | |
|---|---|
| Comparison groups | Lidocaine 5% medicated plaster v Matching Placebo |
| Number of subjects included in analysis | 359 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1533 ^[3] |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.69 |
| upper limit | 0.22 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.23 |

Notes:

[3] - One-sided p-value

Primary: Change of the 24-hours average pain intensity from baseline to week 12_ Subgroup analysis

| | |
|-----------------|---|
| End point title | Change of the 24-hours average pain intensity from baseline to week 12_ Subgroup analysis |
|-----------------|---|

End point description:

The primary efficacy endpoint was the change from baseline of the recorded average pain intensity values during the last 24 hours, averaged over the 7 days of Week 12 of the Double-blind Treatment Period.

The 24-hours pain intensity has been assessed once daily before plaster removal using an 11-point numeric rating scale where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine". The baseline value was defined as the calculated mean of the average pain values during the last 24 hours for the last 7 days of the Enrollment Period.

Missing weekly average pain values have been imputed using the multiple imputation (MI) method.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Week 12 | |

| End point values | Add-on subjects_Lidocaine 5% medicated plaster | Add-on subjects_Matching Placebo | Plaster only subjects_Lidocaine 5% medicated plaster | Plaster only subjects_Matching Placebo |
|-------------------------------------|--|----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 91 ^[4] | 96 ^[5] | 88 ^[6] | 84 ^[7] |
| Units: units on a scale | | | | |
| least squares mean (standard error) | -1.56 (± 0.23) | -1.55 (± 0.22) | -1.87 (± 0.23) | -1.36 (± 0.24) |

Notes:

[4] - Subgroup of the Full Analysis Set using Multiple Imputation Method

[5] - Subgroup of the Full Analysis Set using Multiple Imputation Method

[6] - Subgroup of the Full Analysis Set using Multiple Imputation Method

[7] - Subgroup of the Full Analysis Set using Multiple Imputation Method

Statistical analyses

| Statistical analysis title | ANCOVA using MI method_ Add-on subjects |
|----------------------------|---|
|----------------------------|---|

Statistical analysis description:

An analysis of covariance (ANCOVA) was performed including treatment and concomitant treatment status as factors, and the baseline pain intensity as a covariate using change from baseline on an 11-point NRS as dependent variable. Treatment effects was estimated based on least-squares means (LSmeans) of the difference between Lidocaine Plaster Arm and Placebo Arm and presented together with the corresponding 95% confidence interval (CI) for the treatment comparison.

| | |
|---|---|
| Comparison groups | Add-on subjects_Lidocaine 5% medicated plaster v Add-on subjects_Matching Placebo |
| Number of subjects included in analysis | 187 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.64 |
| upper limit | 0.61 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.32 |

| Statistical analysis title | ANCOVA using MI method_ Plaster only subjects |
|----------------------------|---|
|----------------------------|---|

Statistical analysis description:

An analysis of covariance (ANCOVA) was performed including treatment and concomitant treatment status as factors, and the baseline pain intensity as a covariate using change from baseline on an 11-point NRS as dependent variable. Treatment effects was estimated based on least-squares means (LSmeans) of the difference between Lidocaine Plaster Arm and Placebo Arm and presented together

with the corresponding 95% confidence interval (CI) for the treatment comparison.

| | |
|---|---|
| Comparison groups | Plaster only subjects_Lidocaine 5% medicated plaster v Plaster only subjects_Matching Placebo |
| Number of subjects included in analysis | 172 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -0.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.16 |
| upper limit | 0.14 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 0.33 |

Secondary: Mean pain intensity and mean pain intensity change from baseline based on the 24-hour average pain intensity

| | |
|-----------------|--|
| End point title | Mean pain intensity and mean pain intensity change from baseline based on the 24-hour average pain intensity |
|-----------------|--|

End point description:

Mean pain intensity and mean pain intensity change from baseline based on the average pain intensity during the last 24 hours, calculated over the last 28 days (4 weeks) and 84 days (12 weeks) of the Double-blind Treatment Period.

The subject scored their average pain intensity during the last 24 hours on an 11-point NRS where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine".

The pain intensity has been assessed once daily before plaster removal.

Mean pain intensity and mean pain intensity change from baseline have been summarized descriptively.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

The last 28 days (4 weeks) and 84 days (12 weeks) of the Double-blind Treatment Period.

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|---|--------------------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[8] | 180 ^[9] | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (N = 179; N = 180) | 6.66 (± 1.41) | 6.47 (± 1.38) | | |
| Averaged over the last 4 weeks (N = 143; N = 141) | 5 (± 2.25) | 4.97 (± 2.45) | | |
| Averaged over the 12 weeks (N = 151; N = 156) | 5.4 (± 1.88) | 5.31 (± 2.06) | | |
| Change to 4 weeks average (N =143; N =141) | -1.61 (± 2.02) | -1.49 (± 2.07) | | |
| Change to 12 weeks average (N =151; N =156) | -1.22 (± 1.55) | -1.14 (± 1.58) | | |

Notes:

[8] - Full Analysis Set

[9] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Mean pain intensity and mean pain intensity change from baseline based on the current pain intensity

| | |
|-----------------|--|
| End point title | Mean pain intensity and mean pain intensity change from baseline based on the current pain intensity |
|-----------------|--|

End point description:

Mean pain intensity and mean pain intensity change from baseline based on the current pain intensity before plaster removal, calculated over the last 7 days, 28 days (4 weeks), and 84 days (12 weeks) of the Double-blind Treatment Period.

The subject scored their current pain intensity on an 11-point NRS where a score of 0 indicated "no pain" and a score of 10 indicated "pain as bad as you can imagine".

The current pain intensity before plaster removal has been assessed once daily.

Mean pain intensity and mean pain intensity change from baseline have been summarized descriptively.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Last 7 days, 28 days (4 weeks), and 84 days (12 weeks) of the Double blind Treatment Period

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|---|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[10] | 180 ^[11] | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (N =179; N = 180) | 6.46 (± 1.56) | 6.34 (± 1.5) | | |
| Averaged over the last week (N =122; N =115) | 4.56 (± 2.4) | 4.96 (± 2.55) | | |
| Averaged over the last 4 weeks (N =133; N =127) | 4.65 (± 2.33) | 4.9 (± 2.51) | | |
| Averaged over the 12 weeks (N =140; N =141) | 4.95 (± 1.97) | 5.18 (± 2.22) | | |
| Change to last week average (N =122; N =115) | -1.88 (± 2.23) | -1.48 (± 1.94) | | |
| Change to 4 weeks average (N =133; N =127) | -1.75 (± 2.11) | -1.48 (± 1.98) | | |
| Change to 12 weeks average (N =140; N =141) | -1.43 (± 1.64) | -1.23 (± 1.64) | | |

Notes:

[10] - Full Analysis Set

[11] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Weekly mean pain intensities and weekly mean pain intensity change from baseline based on the 24-hour average pain intensity before plaster removal

| | |
|-----------------|---|
| End point title | Weekly mean pain intensities and weekly mean pain intensity change from baseline based on the 24-hour average pain intensity before plaster removal |
|-----------------|---|

End point description:

Weekly mean pain intensities and weekly mean pain intensity change from baseline based on the 24-hour average pain intensity calculated for each of the 12 weeks of the Double-blind Treatment Period.

Pain intensity has been assessed once daily before plaster removal.

The subject scored their pain intensity 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".

Mean pain intensity and weekly mean pain intensity change from baseline have been summarized descriptively.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Each of the 12 weeks of the Double blind Treatment Period

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|---|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[12] | 180 ^[13] | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (N = 179; N = 180) | 6.66 (± 1.41) | 6.47 (± 1.38) | | |
| Week 1 (N= 170; N= 175) | 6.16 (± 1.59) | 6 (± 1.59) | | |
| Week 2 (N= 168; N= 169) | 5.88 (± 1.76) | 5.69 (± 1.82) | | |
| Week 3 (N= 164; N= 171) | 5.71 (± 1.91) | 5.54 (± 2) | | |
| Week 4 (N= 158; N= 167) | 5.53 (± 2.02) | 5.46 (± 2.05) | | |
| Week 5 (N= 157; N= 159) | 5.46 (± 2) | 5.36 (± 2.17) | | |
| Week 6 (N= 147; N= 155) | 5.39 (± 2.01) | 5.27 (± 2.28) | | |
| Week 7 (N= 144; N=147) | 5.3 (± 2.09) | 5.21 (± 2.28) | | |
| Week 8 (N= 145; N= 150) | 5.3 (± 2.17) | 5.18 (± 2.39) | | |
| Week 9 (N= 140; N= 142) | 5.18 (± 2.29) | 5.11 (± 2.42) | | |
| Week 10 (N= 141; N= 140) | 5.02 (± 2.31) | 5.11 (± 2.43) | | |
| Week 11 (N= 137; N= 135) | 5.06 (± 2.31) | 4.97 (± 2.51) | | |
| Week 12 (N= 129; N= 130) | 4.88 (± 2.32) | 4.94 (± 2.52) | | |
| Change from baseline to week 1 (N= 170; N= 175) | -0.48 (± 1.01) | -0.45 (± 1.01) | | |
| Change from baseline to week 2 (N= 168; N=169) | -0.75 (± 1.24) | -0.74 (± 1.28) | | |
| Change from baseline to week 3 (N= 164; N=171) | -0.95 (± 1.54) | -0.9 (± 1.47) | | |
| Change from baseline to week 4 (N= 158; N= 167) | -1.13 (± 1.75) | -0.98 (± 1.56) | | |
| Change from baseline to week 5 (N= 157; N=159) | -1.15 (± 1.73) | -1.12 (± 1.71) | | |
| Change from baseline to week 6 (N= 147; N= 155) | -1.26 (± 1.8) | -1.17 (± 1.88) | | |
| Change from baseline to week 7 (N= 144; N= 147) | -1.39 (± 1.88) | -1.27 (± 1.82) | | |
| Change from baseline to week 8 (N= 145; N= 150) | -1.36 (± 1.93) | -1.32 (± 1.92) | | |

| | | | | |
|--|----------------|----------------|--|--|
| Change from baseline to week 9 (N= 140; N= 142) | -1.51 (± 2.03) | -1.37 (± 1.99) | | |
| Change from baseline to week 10 (N= 141; N=140) | -1.6 (± 2.1) | -1.39 (± 2.08) | | |
| Change from baseline to week 11 (N= 137; N= 135) | -1.57 (± 2.08) | -1.48 (± 2.1) | | |
| Change from baseline to Week 12 (N= 129; N= 130) | -1.78 (± 2.15) | -1.54 (± 2.11) | | |

Notes:

[12] - Full Analysis Set

[13] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Weekly mean pain intensities and weekly mean pain intensity change based on current pain intensity before plaster removal

| | |
|-----------------|---|
| End point title | Weekly mean pain intensities and weekly mean pain intensity change based on current pain intensity before plaster removal |
|-----------------|---|

End point description:

Weekly mean pain intensities and weekly mean pain intensity change from baseline based on the current pain intensity before plaster removal calculated for each of the 12 weeks of the Double-blind Treatment Period.

The subject scored their current pain intensity 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 current pain intensity has been assessed once daily before plaster removal.

Mean pain intensity and weekly mean pain intensity change from baseline have been summarized descriptively.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Each of the 12 weeks of the Double blind Treatment Period

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|--------------------------------------|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[14] | 180 ^[15] | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (N = 179; N = 180) | 6.46 (± 1.56) | 6.34 (± 1.5) | | |
| Week 1 (N= 158; N= 161) | 5.73 (± 1.82) | 5.77 (± 1.75) | | |
| Week 2 (N= 154; N= 152) | 5.47 (± 1.96) | 5.46 (± 1.99) | | |
| Week 3 (N= 154; N= 159) | 5.2 (± 2.07) | 5.37 (± 2.12) | | |
| Week 4 (N= 148; N= 155) | 5.08 (± 2.18) | 5.26 (± 2.19) | | |
| Week 5 (N= 142; N= 144) | 5.11 (± 2.05) | 5.27 (± 2.24) | | |
| Week 6 (N= 134; N= 141) | 4.98 (± 2.11) | 5.18 (± 2.32) | | |
| Week 7 (N= 131; N=134) | 4.95 (± 2.24) | 5.09 (± 2.42) | | |
| Week 8 (N= 133; N= 139) | 4.92 (± 2.28) | 5.08 (± 2.43) | | |
| Week 9 (N= 127; N= 132) | 4.81 (± 2.36) | 5.04 (± 2.46) | | |
| Week 10 (N= 131; N= 127) | 4.59 (± 2.36) | 5.02 (± 2.48) | | |
| Week 11 (N= 126; N= 123) | 4.57 (± 2.41) | 4.86 (± 2.58) | | |
| Week 12 (N= 122; N= 115) | 4.56 (± 2.4) | 4.96 (± 2.55) | | |

| | | | | |
|--|----------------|----------------|--|--|
| Change from baseline to week 1 (N= 158; N= 161) | -0.73 (± 1.21) | -0.57 (± 1.18) | | |
| Change from baseline to week 2 (N= 154; N= 152) | -0.97 (± 1.42) | -0.89 (± 1.45) | | |
| Change from baseline to week 3 (N= 154; N= 159) | -1.24 (± 1.61) | -1.03 (± 1.54) | | |
| Change from baseline to week 4 (N= 148; N= 155) | -1.36 (± 1.85) | -1.12 (± 1.6) | | |
| Change from baseline to week 5 (N= 142; N= 144) | -1.32 (± 1.85) | -1.16 (± 1.7) | | |
| Change from baseline to week 6 (N= 134; N= 141) | -1.4 (± 1.9) | -1.2 (± 1.87) | | |
| Change from baseline to week 7 (N= 131; N= 134) | -1.5 (± 2.04) | -1.33 (± 1.88) | | |
| Change from baseline to week 8 (N= 133; N= 139) | -1.53 (± 2.12) | -1.33 (± 1.91) | | |
| Change from baseline to week 9 (N= 127; N= 132) | -1.62 (± 2.09) | -1.38 (± 1.92) | | |
| Change from baseline to week 10 (N= 131; N= 127) | -1.78 (± 2.18) | -1.42 (± 1.99) | | |
| Change from baseline to week 11 (N= 126; N= 123) | -1.84 (± 2.22) | -1.51 (± 2.03) | | |
| Change from baseline to week 12 (N= 122; N= 115) | -1.88 (± 2.23) | -1.48 (± 1.94) | | |

Notes:

[14] - Full Analysis Set

[15] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Responder rates based on average pain intensity values during the last 24 hours at the end of the Double-blind Treatment Period

| | |
|-----------------|---|
| End point title | Responder rates based on average pain intensity values during the last 24 hours at the end of the Double-blind Treatment Period |
|-----------------|---|

End point description:

The percentage change from baseline of the average pain intensity values during the last 24 hours at the end of the Double-blind Treatment Period has been calculated for each subject.

Responders are defined as subjects with at least 30% or 50% reduction. All discontinued subjects were considered non-responders except for those who did not require pain treatment any more due to absence of pain.

Responder rates (thresholds of 30% and 50% improvement compared to baseline) have been descriptively summarized.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

The last 24 hours at the end of the Double blind Treatment Period

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|-----------------------------|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[16] | 180 ^[17] | | |
| Units: subjects | | | | |

| | | | | |
|--|----|----|--|--|
| Responder with more or equal of 30% pain reduction | 41 | 45 | | |
| Responder with more or equal of 50% pain reduction | 13 | 19 | | |

Notes:

[16] - Full Analysis Set

[17] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Final score of the painDETECT Pain Questionnaire and the changes from baseline during the Double-blind Treatment Period

| | |
|-----------------|---|
| End point title | Final score of the painDETECT Pain Questionnaire and the changes from baseline during the Double-blind Treatment Period |
|-----------------|---|

End point description:

The painDETECT questionnaire was specifically developed to detect neuropathic pain components in adult patients with low back pain.

The questionnaire consists of seven questions that address the quality of neuropathic pain symptoms with a final score between zero and 38.

A higher score shows more likelihood of a neuropathic pain component.

The final score and the changes from baseline during the Double-blind Treatment Period have been summarized.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 3 (week 4), visit 4 (week 8) and visit 5 (week 12; End-of treatment/Discontinuation Visit) of the Double blind Treatment Period.

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|--|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[18] | 180 ^[19] | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (N =177; N = 180) | 20.8 (± 5.3) | 21.5 (± 5.6) | | |
| Visit 3 (N= 157; N= 160) | 17.8 (± 7) | 18.1 (± 7) | | |
| Visit 4 (N= 145; N= 146) | 16.9 (± 7.3) | 16.8 (± 7.7) | | |
| Visit 5 (N= 174; N= 167) | 16.4 (± 8) | 16.6 (± 8.3) | | |
| Change from baseline to visit 3 (N= 157; N= 160) | -2.9 (± 5.2) | -3.4 (± 5) | | |
| Change from baseline to visit 4 (N= 145; N= 146) | -3.9 (± 5.7) | -4.9 (± 6.2) | | |
| Change from baseline to visit 5 (N= 174; N= 167) | -4.4 (± 6.3) | -5 (± 6.7) | | |

Notes:

[18] - Full Analysis Set

[19] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Pain intensity from mechanical dynamic allodynia (brush) testing and change from baseline

| | |
|---|---|
| End point title | Pain intensity from mechanical dynamic allodynia (brush) testing and change from baseline |
| End point description: The test has been conducted by means of a brush provided by the sponsor. The skin in PoNP area has been repeatedly lightly stroked with a brush with an interval of more than 5 seconds between the strokes. The intensity of the pain has been assessed by subject and the highest severity of the pain has been rated using the 11-point NRS. Pain intensity from mechanical dynamic allodynia (brush) testing and change from baseline has been summarized. | |
| End point type | Secondary |
| End point timeframe: Visit 3 (week 4), visit 4 (week 8) and visit 5 (week 12; End-of treatment/Discontinuation Visit) of the Double blind Treatment Period | |

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|--|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[20] | 180 ^[21] | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (N= 178; N= 180) | 6.2 (± 2.1) | 6.1 (± 2.3) | | |
| Visit 3 (N= 159; N= 164) | 4.8 (± 2.4) | 4.9 (± 2.6) | | |
| Visit 4 (N= 146; N= 148) | 4.7 (± 2.7) | 4.6 (± 2.8) | | |
| Visit 5 (N= 175; N= 176) | 4.7 (± 2.7) | 4.7 (± 2.8) | | |
| Change from baseline to visit 3 (N= 158; N= 164) | -1.3 (± 2.2) | -1.2 (± 2) | | |
| Change from baseline to visit 4 (N= 145; N= 148) | -1.5 (± 2.5) | -1.6 (± 2.7) | | |
| Change from baseline to visit 5 (N= 174; N=176) | -1.5 (± 2.6) | -1.3 (± 2.5) | | |

Notes:

[20] - Full Analysis Set

[21] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Anxiety and depression scores of HADS and changes from baseline

| | |
|---|---|
| End point title | Anxiety and depression scores of HADS and changes from baseline |
| End point description: The Hospital Anxiety and Depression Scale (HADS) is a 14-item self-assessment scale for detecting states of depression and anxiety. It contains 2 subscales, one for anxiety and one for depression, each consisting of 7 items. Each subscale consists of 7 statements, rated on a scale of 0 to 3 (0 = No anxiety or depression, to 3 = Severe feelings of anxiety or depression), resulting in a range for each dimension from 0-21. Higher scores denote greater severity of depression or anxiety. The 2 subscores have been calculated as the sum of corresponding items | |
| End point type | Secondary |

End point timeframe:

Visit 5 (week 12; End-of treatment/Discontinuation Visit) of the Double blind Treatment Period

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|---|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 170 ^[22] | 180 ^[23] | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Anxiety_ Baseline (N=178; N= 178) | 8.8 (± 4.5) | 9.3 (± 4.8) | | |
| Anxiety_Visit 5 (N=174; N= 172) | 7.7 (± 4.7) | 8 (± 4.8) | | |
| Anxiety_ Change from baseline (N=174; N=170) | -1.1 (± 3.5) | -1.3 (± 3.2) | | |
| Depression_ Baseline (N=178, N=178) | 7 (± 4.2) | 7.6 (± 4.5) | | |
| Depression_V5 (N=174; N=172) | 6.3 (± 4.4) | 7.1 (± 4.7) | | |
| Depression_ Change from baseline (N=174; N=170) | -0.7 (± 3.3) | -0.5 (± 3.3) | | |

Notes:

[22] - Full Analysis Set

[23] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Rating of global improvement and satisfaction with treatment according to PGIC

| | |
|-----------------|--|
| End point title | Rating of global improvement and satisfaction with treatment according to PGIC |
|-----------------|--|

End point description:

Subjects rated their global improvement and satisfaction with treatment on a 7-point scale that ranges from "very much improved" to "very much worse" with "no change" as the mid-point. The results have been summarized.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 5 (week 12; End-of treatment/Discontinuation Visit) of the Double blind Treatment Period

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|-----------------------------|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[24] | 180 ^[25] | | |
| Units: subjects | | | | |
| Not Done | 4 | 6 | | |
| Very much improved | 11 | 20 | | |
| Much improved | 52 | 42 | | |
| Minimally improved | 47 | 40 | | |
| No change | 49 | 55 | | |

| | | | | |
|-----------------|----|----|--|--|
| Minimally worse | 11 | 12 | | |
| Much worse | 5 | 4 | | |
| Very much worse | 0 | 0 | | |
| Missing | 0 | 1 | | |

Notes:

[24] - Full Analysis Set

[25] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: The weighted Health Status Index of quality of life by means of EuroQol-5 Dimension

| | |
|-----------------|---|
| End point title | The weighted Health Status Index of quality of life by means of EuroQol-5 Dimension |
|-----------------|---|

End point description:

The EQ 5D Health Questionnaire is a generic health related quality of life instrument which can be used in the clinical and economic evaluation of healthcare and in population health surveys to assess health outcome from a wide variety of interventions.

The EQ-5D has 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has been scored as followed: no problems = 1, some problems = 2, and extreme problems = 3.

A higher score in the Weighted Health Status Index indicates an improvement in health.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 5 (week 12; End-of treatment/Discontinuation Visit) of the Double blind Treatment Period.

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|--|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[26] | 180 ^[27] | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (N= 178; N= 178) | 0.397 (± 0.321) | 0.392 (± 0.334) | | |
| Visit 5 (N= 175; N= 169) | 0.497 (± 0.313) | 0.495 (± 0.322) | | |
| Change from baseline to visit 5 (N= 174; N= 167) | 0.098 (± 0.282) | 0.107 (± 0.281) | | |

Notes:

[26] - Full Analysis Set

[27] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Total score in quality of sleep using CPSI and change from baseline

| | |
|-----------------|---|
| End point title | Total score in quality of sleep using CPSI and change from baseline |
|-----------------|---|

End point description:

The Impact of pain on sleep quality has been assessed by the Chronic Pain Sleep Inventory (CPSI). The CPSI consists of 5 items which measure trouble falling asleep, needing sleep medication, awakened by pain during the night and in the morning, and overall quality of sleep on a 100 mm visual analog scale. The total score and change from baseline have been summarized descriptively. A higher score indicates more sleeping problems.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Visit 5 (week 12; End-of treatment/Discontinuation Visit) of the Double blind Treatment Period

| End point values | Lidocaine 5% medicated plaster | Matching Placebo | | |
|--|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 179 ^[28] | 180 ^[29] | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Sleep Problem Index Baseline (N = 176; N = 179) | 161.9 (± 86.9) | 153.4 (± 89.8) | | |
| Sleep Problem Index Visit 5 (N= 173; N= 171) | 122.8 (± 89.6) | 110.1 (± 95.5) | | |
| Change from baseline to visit 5 (N= 170; N= 170) | -38.7 (± 78.4) | -43.3 (± 91.2) | | |

Notes:

[28] - Full Analysis Set

[29] - Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Responder rates based on average pain intensity values during the last 24 hours at the end of the Double-blind Treatment Period__ Subgroup analysis

| | |
|-----------------|---|
| End point title | Responder rates based on average pain intensity values during the last 24 hours at the end of the Double-blind Treatment Period__ Subgroup analysis |
|-----------------|---|

End point description:

The percentage change from baseline of the average pain intensity values during the last 24 hours at the end of the Double-blind Treatment Period has been calculated for each subject.

Responders are defined as subjects with at least 30% or 50% reduction. All discontinued subjects were considered non-responders except for those who did not require pain treatment any more due to absence of pain.

Responder rates (thresholds of 30% and 50% improvement compared to baseline) have been descriptively summarized.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

The last 24 hours at the end of the Double blind Treatment Period

| End point values | Add-on subjects_Lidoc aine 5% medicated plaster | Add-on subjects_ Matching Placebo | Plaster only subjects_Lidoc aine 5% medicated plaster | Plaster only subjects_Match ing Placebo |
|---|---|--|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 91 ^[30] | 96 ^[31] | 88 ^[32] | 84 ^[33] |
| Units: Subjects | | | | |
| Responder with more or equal of 30% pain reduction | 19 | 26 | 22 | 19 |
| Responder with more or equal of 50% pain reduction | 8 | 12 | 5 | 7 |

Notes:

[30] - Subgroup of the Full Analysis Set

[31] - Subgroup of the Full Analysis Set

[32] - Subgroup of the Full Analysis Set

[33] - Subgroup of the Full Analysis Set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment Emergent Adverse Events (TEAEs) reported include all Adverse Events occurring after first application of investigational medicinal product (IMP) up to and including Visit 6 (end of double-blind treatment, i.e. up to 12 weeks).

Adverse event reporting additional description:

Events present at enrollment were considered medical history. Events that worsened between enrollment and first application of plaster were Adverse Events, but not Treatment Emergent Adverse Events.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 19.0 |

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | Lidocaine 5% medicated plaster |
|-----------------------|--------------------------------|

Reporting group description:

This arm comprises all subjects allocated to lidocaine 5% medicated plaster who applied any amount of IMP.

Subjects were analyzed as administered, i.e., based on actual treatment received.

| | |
|-----------------------|------------------|
| Reporting group title | Matching Placebo |
|-----------------------|------------------|

Reporting group description:

This arm comprises all subjects allocated to placebo plaster who applied any amount of IMP.

Subjects were analyzed as administered, i.e., based on actual treatment received.

| Serious adverse events | Lidocaine 5% medicated plaster | Matching Placebo | |
|---|---|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 179 (3.35%) | 5 / 180 (2.78%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Thoracic vertebral fracture | Additional description: verbatim text: Thoracic vertebral fracture TH11 | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 180 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post-traumatic pain | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 180 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fractured sacrum | | | |

| | | | |
|---|--|-----------------|--|
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 180 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 180 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 180 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Sciatica | | | |
| subjects affected / exposed | 2 / 179 (1.12%) | 1 / 180 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 0 / 179 (0.00%) | 1 / 180 (0.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicide attempt | | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 180 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteoarthritis | Additional description: verbatim text: shock wave therapy right shoulder | | |
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 180 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Urinary tract infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 179 (0.56%) | 0 / 180 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Lidocaine 5% medicated plaster | Matching Placebo | |
|---|-----------------------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 23 / 179 (12.85%) | 15 / 180 (8.33%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 10 / 179 (5.59%) | 8 / 180 (4.44%) | |
| occurrences (all) | 13 | 8 | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 13 / 179 (7.26%) | 7 / 180 (3.89%) | |
| occurrences (all) | 13 | 8 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|---|
| 15 July 2014 | This amendment was mainly issued to modify inclusion/exclusion criteria and to specify further the reporting requirements for medical history. Furthermore, for the analysis of the primary endpoint and the definition of the analysis populations, the wording changes were necessary for clarity. In addition, the planned sensitivity analyses were changed to comply with recommendations given in The National Academy of Sciences report on "The Prevention and Treatment of Missing Data in Clinical Trials" commissioned by the FDA. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported