



Clinical trial results:

Randomized, controlled, multi-center trial to evaluate the efficacy and safety of Lixim 70 mg wirkstoffhaltiges Pflaster (etofenamate 70 mg medicated plaster) vs. placebo in the local symptomatic and short-term treatment of pain in acute strains, sprains or bruises of soft tissues following blunt trauma, e.g. sports injuries

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2021-003778-30 |
| Trial protocol | DE |
| Global end of trial date | 28 September 2022 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 11 April 2024 |
| First version publication date | 11 April 2024 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | DRO-200/III/21/1 |
|-----------------------|------------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Drossapharm AG |
| Sponsor organisation address | Birsweg 1, Arlesheim, Switzerland, 4144 |
| Public contact | Prof. Dr. Giannetti, Clinsearch GmbH, 41 417116376, info@clinsearch.de |
| Scientific contact | Prof. Dr. Giannetti, Clinsearch GmbH, 41 417116376, info@clinsearch.de |

Notes:

Paediatric regulatory details

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|--|----|
| 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 | 17 November 2023 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 September 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that the Lixim plaster applied once every 24 hours is superior to matching placebo plasters, in particular with regard to pain relief, in patients with acute strains, sprains or bruises (contusions) of the soft tissues following blunt trauma, e.g., sports injuries.

Protection of trial subjects:

This clinical trial was designed, implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice, with applicable local regulations (including applicable European Directives, AMG and GCP-V), and with the ethical principles laid down in the Declaration of Helsinki. The clinical trial was initiated after written and dated positive vote by the IEC and approval by the national health authority (BfArM) were received for the documents required by the GCP regulation including clinical trial protocol, subject information including the ICF as well as any subsequent amendments. Eligible patients were only included in the clinical trial after providing written (witnessed, where required by law or regulation), IEC-approved informed consent. Informed consent was obtained before conducting any clinical trial-specific procedures (i.e., all the procedures described in the protocol). The process of obtaining informed consent was documented in the patient source documents. Every patient received an information sheet on insurance coverage together with a copy of the patient information and signed informed consent. Patients could voluntarily withdraw from the clinical trial for any reason at any time. Women of child bearing potential were informed that taking the IMP may involve unknown risks to the foetus if pregnancy occurred during the clinical trial and agreed that in order to participate in the clinical trial, they had to adhere to the contraception requirement for the duration of the clinical trial. If there was any question that the patient might not reliably comply, they were not to be entered in the clinical trial.

Background therapy: -

Evidence for comparator:

None.

| | |
|---|---------------|
| Actual start date of recruitment | 15 March 2022 |
| 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 | Germany: 180 |
| Worldwide total number of subjects | 180 |
| EEA total number of subjects | 180 |

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) | 176 |
| From 65 to 84 years | 4 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A randomization visit (baseline visit) was performed directly before the administration of the investigational medicinal product at visit 1.

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:

Patients, Investigator staff, assessors, monitors and data analysts remained blinded to the identity of the treatment (active or placebo) from the time of randomization until database lock. Methods: (1) randomization data were kept strictly confidential, accessible only to authorized persons, until the time of unblinding; (2) the identity of the treatments was concealed by the use of IMPs that were all identical in packaging, labelling, schedule of administration, appearance and odour.

Arms

| | |
|--|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Lixim patch |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Lixim 70 mg wirkstoffhaltiges Pflaster |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cutaneous patch |
| Routes of administration | Cutaneous use, Topical use |

Dosage and administration details:

One "Lixim 70 mg wirkstoffhaltiges Pflaster" was applied every 24 h throughout the 7 days treatment period.

Patients were instructed to apply the plaster in the center of the cleaned and dried injured area. The applied plaster was pressed to the skin for at least 30-60 sec to guarantee optimal plaster adhesion. The patients were instructed to continue to apply the plaster once a day every 24 hours, for 7 days until the final visit.

| | |
|--|----------------------------|
| Arm title | Placebo patch |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo patch |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cutaneous patch |
| Routes of administration | Cutaneous use, Topical use |

Dosage and administration details:

One placebo patch was applied every 24 h throughout the 7 days treatment period.

Patients were instructed to apply the plaster in the center of the cleaned and dried injured area. The applied plaster was pressed to the skin for at least 30-60 sec to guarantee optimal plaster adhesion. The patients were instructed to continue to apply the plaster once a day every 24 hours, for 7 days until the final visit.

| Number of subjects in period 1 | Lixim patch | Placebo patch |
|---------------------------------------|-------------|---------------|
| Started | 120 | 60 |
| Completed | 120 | 60 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Lixim patch |
| Reporting group description: - | |
| Reporting group title | Placebo patch |
| Reporting group description: - | |

| Reporting group values | Lixim patch | Placebo patch | Total |
|---------------------------------------|-------------|---------------|-------|
| Number of subjects | 120 | 60 | 180 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 116 | 60 | 176 |
| From 65-84 years | 4 | 0 | 4 |
| Age continuous Units: years | | | |
| arithmetic mean | 36.5 | 30.6 | |
| standard deviation | ± 14.1 | ± 11.4 | - |
| Gender categorical Units: Subjects | | | |
| Female | 61 | 28 | 89 |
| Male | 59 | 32 | 91 |

End points

End points reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Lixim patch |
| Reporting group description: - | |
| Reporting group title | Placebo patch |
| Reporting group description: - | |

Primary: Pain intensity difference (PID)

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|---|---------------------------------|
| End point title | Pain intensity difference (PID) |
| End point description: The primary efficacy variable was the pain intensity difference (PID) in pain-on-movement (POM) assessed at visit 5 (72 hours after initiating treatment). POM was assessed by standardised procedures involving a movement of the injured limb and the assessment of the level of patient-reported pain experienced during the movement via the 100 mm VAS scale from 0 = "no pain" to 100 = "Extreme pain". From POM values the PID was calculated by subtracting POM VAS from baseline, so that greater negative PID values indicate greater pain reduction. | |
| End point type | Primary |
| End point timeframe: Visit 5 (72 hours after initiating treatment) | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: millimeter | | | | |
| arithmetic mean (standard deviation) | -58.9 (± 11.1) | -33.3 (± 15.5) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison for test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -28.6833 |
| upper limit | -21.3408 |

Secondary: Pain-on-movement (POM) change from baseline (PID) to visit 2

| | |
|--|--|
| End point title | Pain-on-movement (POM) change from baseline (PID) to visit 2 |
| End point description: VAS-based PID values for Pain-on-movement (POM) were also assessed – in addition to visit 5 – throughout the conduct of the study at Visits 2, 3, 4, 6, 7 and 8. | |
| End point type | Secondary |
| End point timeframe: change from baseline (PID) to visit 2 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -11.8 (± 9.8) | -7.4 (± 7.7) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.4006 |
| upper limit | -2.1322 |
| Variability estimate | Standard error of the mean |

Secondary: Pain-on-movement (POM) change from baseline (PID) to visit 3

| | |
|--|--|
| End point title | Pain-on-movement (POM) change from baseline (PID) to visit 3 |
| End point description: VAS-based PID values for Pain-on-movement (POM) were also assessed – in addition to visit 5 – throughout the conduct of the study at Visits 2, 3, 4, 6, 7 and 8. | |
| End point type | Secondary |
| End point timeframe: change from baseline (PID) to visit 3 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -25.6 (± 15.7) | -14.2 (± 11.4) | | |

Statistical analyses

| Statistical analysis title | Treatment comparison - Test vs. placebo |
|---|---|
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.3704 |
| upper limit | -7.5155 |
| Variability estimate | Standard error of the mean |

Secondary: Pain-on-movement (POM) change from baseline (PID) to visit 4

| | |
|------------------------|--|
| End point title | Pain-on-movement (POM) change from baseline (PID) to visit 4 |
| End point description: | VAS-based PID values for Pain-on-movement (POM) were also assessed – in addition to visit 5 – throughout the conduct of the study at Visits 2, 3, 4, 6, 7 and 8. |
| End point type | Secondary |
| End point timeframe: | change from baseline (PID) to visit 4 |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -46.1 (± 13.8) | -23.7 (± 14.4) | | |

Statistical analyses

| Statistical analysis title | Treatment comparison - Test vs. placebo |
|----------------------------|---|
| Comparison groups | Lixim patch v Placebo patch |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -25.8862 |
| upper limit | -17.9354 |
| Variability estimate | Standard error of the mean |

Secondary: Pain-on-movement (POM) change from baseline (PID) to visit 6

| | |
|------------------------|--|
| End point title | Pain-on-movement (POM) change from baseline (PID) to visit 6 |
| End point description: | VAS-based PID values for Pain-on-movement (POM) were also assessed – in addition to visit 5 – throughout the conduct of the study at Visits 2, 3, 4, 6, 7 and 8. |
| End point type | Secondary |
| End point timeframe: | change from baseline (PID) to visit 6 |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -65.2 (± 9.5) | -42.0 (± 16.4) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -25.9338 |
| upper limit | -18.9431 |
| Variability estimate | Standard error of the mean |

Secondary: Pain-on-movement (POM) change from baseline (PID) to visit 7

| | |
|-----------------|--|
| End point title | Pain-on-movement (POM) change from baseline (PID) to visit 7 |
|-----------------|--|

End point description:

VAS-based PID values for Pain-on-movement (POM) were also assessed – in addition to visit 5 – throughout the conduct of the study at Visits 2, 3, 4, 6, 7 and 8.

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

End point timeframe:

change from baseline (PID) to visit 7

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -67.7 (± 8.6) | -52.1 (± 16.0) | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
|----------------------------|---|

| | |
|-------------------|-----------------------------|
| Comparison groups | Lixim patch v Placebo patch |
|-------------------|-----------------------------|

| | |
|---|-----|
| Number of subjects included in analysis | 180 |
|---|-----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

| | |
|---------|----------|
| P-value | < 0.0001 |
|---------|----------|

| | |
|--------|--------|
| Method | ANCOVA |
|--------|--------|

Confidence interval

| | |
|-------|------|
| level | 95 % |
|-------|------|

| | |
|-------|---------|
| sides | 2-sided |
|-------|---------|

| | |
|-------------|----------|
| lower limit | -18.2083 |
|-------------|----------|

| | |
|-------------|----------|
| upper limit | -11.5272 |
|-------------|----------|

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
|----------------------|----------------------------|

Secondary: Pain-on-movement (POM) change from baseline (PID) to visit 8

| | |
|-----------------|--|
| End point title | Pain-on-movement (POM) change from baseline (PID) to visit 8 |
|-----------------|--|

End point description:

VAS-based PID values for Pain-on-movement (POM) were also assessed – in addition to visit 5 – throughout the conduct of the study at Visits 2, 3, 4, 6, 7 and 8.

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

End point timeframe:

change from baseline (PID) to visit 8

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -70.0 (± 6.2) | -62.4 (± 13.2) | | |

Statistical analyses

| Statistical analysis title | Treatment comparison - Test vs. placebo |
|---|---|
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.833 |
| upper limit | -4.3986 |
| Variability estimate | Standard error of the mean |

Secondary: AUC for POM on VAS over time between baseline and 24 hours

| | |
|------------------------|--|
| End point title | AUC for POM on VAS over time between baseline and 24 hours |
| End point description: | For POM on VAS, partial AUCs were calculated based on the raw VAS values and actual times of scheduled visits as described in the SAP. |
| End point type | Secondary |
| End point timeframe: | between baseline and 24 hours (visit 3) |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|---------------------------------------|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm*h | | | | |
| arithmetic mean (standard deviation) | 1384.0618056 0 (± 239.18189325) | 1469.6743056 0 (± 216.59710130) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -147.42 |
| upper limit | -67.1408 |
| Variability estimate | Standard error of the mean |

Secondary: AUC for POM on VAS over time between baseline and 48 hours

| | |
|--|--|
| End point title | AUC for POM on VAS over time between baseline and 48 hours |
| End point description: | |
| For POM on VAS, partial AUCs were calculated based on the raw VAS values and actual times of scheduled visits as described in the SAP. | |
| End point type | Secondary |
| End point timeframe: | |
| between baseline and 48 hours (visit 4) | |

| | | | | |
|--------------------------------------|---------------------------------------|---------------------------------------|--|--|
| End point values | Lixim patch | Placebo patch | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm*h | | | | |
| arithmetic mean (standard deviation) | 2183.9923611 0 (± 544.71997353) | 2636.1569444 0 (± 490.04206465) | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| sides | 2-sided |
| lower limit | -602.3 |
| upper limit | -374.95 |
| Variability estimate | Standard error of the mean |

Secondary: AUC for POM on VAS over time between baseline and 72 hours

| | |
|--|--|
| End point title | AUC for POM on VAS over time between baseline and 72 hours |
| End point description: | |
| For POM on VAS, partial AUCs were calculated based on the raw VAS values and actual times of scheduled visits as described in the SAP. | |
| End point type | Secondary |
| End point timeframe: | |
| between baseline and 72 hours (visit 5) | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|---------------------------------------|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm*h | | | | |
| arithmetic mean (standard deviation) | 2609.8493056 0 (± 780.32156579) | 3614.4333333 0 (± 812.76187784) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1241.12 |
| upper limit | -864.75 |
| Variability estimate | Standard error of the mean |

Secondary: AUC for POM on VAS over time between baseline and 96 hours

| | |
|-----------------|--|
| End point title | AUC for POM on VAS over time between baseline and 96 hours |
|-----------------|--|

End point description:

For POM on VAS, partial AUCs were calculated based on the raw VAS values and actual times of scheduled visits as described in the SAP.

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

End point timeframe:

between baseline and 96 hours (visit 6)

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|---------------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm*h | | | | |
| arithmetic mean (standard deviation) | 2808.4614583 0 (± 927.63133296) | 4375.9055556 0 (± 1142.2813188 0) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1879.52 |
| upper limit | -1368.57 |
| Variability estimate | Standard error of the mean |

Secondary: AUC for POM on VAS over time between baseline and 168 hours

| | |
|-----------------|---|
| End point title | AUC for POM on VAS over time between baseline and 168 hours |
|-----------------|---|

End point description:

For POM on VAS, partial AUCs were calculated based on the raw VAS values and actual times of scheduled visits as described in the SAP.

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

End point timeframe:
between baseline and 168 hours (visit 7)

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Lixim patch | Placebo patch | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm*h | | | | |
| arithmetic mean (standard deviation) | 2903.0086806 0 (± 1041.9966214 0) | 4910.1833333 0 (± 1457.1911964 0) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2389.41 |
| upper limit | -1753.43 |
| Variability estimate | Standard error of the mean |

Secondary: Pain-on-movement (POM) Sum of Pain Intensity Differences (SPID) at visit 3

| | |
|---|--|
| End point title | Pain-on-movement (POM) Sum of Pain Intensity Differences (SPID) at visit 3 |
| End point description: | |
| For POM on VAS, the time-weighted sum of pain intensity differences (SPID) was calculated based on the raw VAS values and actual times of scheduled visits as described in the SAP. | |
| End point type | Secondary |
| End point timeframe: | |
| Visit 3 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm*h | | | | |
| arithmetic mean (standard deviation) | -304.33819440 (± 186.18615399) | -193.12569440 (± 146.69903391) | | |

Statistical analyses

| Statistical analysis title | Treatment comparison - Test vs. placebo |
|---|---|
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -147.42 |
| upper limit | -67.1408 |
| Variability estimate | Standard error of the mean |

Secondary: Pain-on-movement (POM) Sum of Pain Intensity Differences (SPID) at visit 4

| | |
|------------------------|---|
| End point title | Pain-on-movement (POM) Sum of Pain Intensity Differences (SPID) at visit 4 |
| End point description: | For POM on VAS, the time-weighted sum of pain intensity differences (SPID) was calculated based on the raw VAS values and actual times of scheduled visits as described in the SAP. |
| End point type | Secondary |
| End point timeframe: | visit 4 |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|---------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm*h | | | | |
| arithmetic mean (standard deviation) | - 1192.8076390 0 (± | -689.44305550 (± 401.47066117) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -602.3 |
| upper limit | -374.95 |
| Variability estimate | Standard error of the mean |

Secondary: Pain-on-movement (POM) Sum of Pain Intensity Differences (SPID) at visit 5

| | |
|---|--|
| End point title | Pain-on-movement (POM) Sum of Pain Intensity Differences (SPID) at visit 5 |
| End point description: | |
| For POM on VAS, the time-weighted sum of pain intensity differences (SPID) was calculated based on the raw VAS values and actual times of scheduled visits as described in the SAP. | |
| End point type | Secondary |
| End point timeframe: | |
| visit 5 | |

| | | | | |
|--------------------------------------|---------------------------|---------------------------|--|--|
| End point values | Lixim patch | Placebo patch | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm*h | | | | |
| arithmetic mean (standard deviation) | - 2455.3506940 0 (± | - 1373.9666670 0 (± | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1241.12 |
| upper limit | -864.75 |
| Variability estimate | Standard error of the mean |

Secondary: Pain-on-movement (POM) Sum of Pain Intensity Differences (SPID) at visit 6

| | |
|---|--|
| End point title | Pain-on-movement (POM) Sum of Pain Intensity Differences (SPID) at visit 6 |
| End point description: | |
| For POM on VAS, the time-weighted sum of pain intensity differences (SPID) was calculated based on the raw VAS values and actual times of scheduled visits as described in the SAP. | |
| End point type | Secondary |
| End point timeframe: | |
| visit 6 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|---------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm*h | | | | |
| arithmetic mean (standard deviation) | - 3945.1385420 0 (± | - 2275.2944440 0 (± 1048.1230634 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |

| | |
|----------------------|----------------------------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1879.52 |
| upper limit | -1368.57 |
| Variability estimate | Standard error of the mean |

Secondary: Pain-on-movement (POM) Sum of Pain Intensity Differences (SPID) at visit 7

| | |
|---|--|
| End point title | Pain-on-movement (POM) Sum of Pain Intensity Differences (SPID) at visit 7 |
| End point description: For POM on VAS, the time-weighted sum of pain intensity differences (SPID) was calculated based on the raw VAS values and actual times of scheduled visits as described in the SAP. | |
| End point type | Secondary |
| End point timeframe: visit 7 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm*h | | | | |
| arithmetic mean (standard deviation) | - 5538.9913190 0 (± 1023.0995730 | - 3403.8166670 0 (± 1364.7671483 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2389.41 |
| upper limit | -1753.43 |
| Variability estimate | Standard error of the mean |

Secondary: Pain-on-movement – Time to meaningful (30 %) reduction

| | |
|-----------------|--|
| End point title | Pain-on-movement – Time to meaningful (30 %) reduction |
|-----------------|--|

End point description:

Time to meaningful reduction of pain was calculated as 30 % reduction of baseline POM, based on the VAS values measured for POM at each of the study visits.

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

End point timeframe:

Descriptive statistics for the time to meaningful reduction

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 59 | | |
| Units: hour | | | | |
| arithmetic mean (standard deviation) | 33.194 (± 20.069) | 60.172 (± 26.638) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pain-on-movement – Time to optimal (50 %) reduction

| | |
|-----------------|---|
| End point title | Pain-on-movement – Time to optimal (50 %) reduction |
|-----------------|---|

End point description:

Time to optimal reduction of pain was calculated as 50 % reduction of baseline POM, based on the VAS values measured for POM at each of the study visits.

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

End point timeframe:

Descriptive statistics

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 58 | | |
| Units: hour | | | | |
| arithmetic mean (standard deviation) | 46.073 (± 21.462) | 94.025 (± 39.710) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pain-on-movement Responder at visit 5 (72h)

| | |
|--|---|
| End point title | Pain-on-movement Responder at visit 5 (72h) |
| End point description: The responder rate 1 was defined as the number of patients achieving at least 50 % reduction from baseline in the VAS score for POM at 72 hours. | |
| End point type | Secondary |
| End point timeframe: at visit 5 (72h) | |

| End point values | Lixim patch | Placebo patch | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: YES | 118 | 23 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Pain at rest (PAR) at visit 2

| | |
|--|-------------------------------|
| End point title | Pain at rest (PAR) at visit 2 |
| End point description: The patients' pain at rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h), V6 (96 h), V7 (120 h) and V8 (7 d) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question: "How would you describe your ankle pain right now?" "Wie würden Sie Ihre Schmerzen in Ihrem Sprunggelenk in diesem Moment beschreiben?" | |
| End point type | Secondary |
| End point timeframe: at visit 2 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -4.2 (± 4.8) | -3.3 (± 4.5) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.225 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.7237 |
| upper limit | 0.4083 |
| Variability estimate | Standard error of the mean |

Secondary: Pain at rest (PAR) at visit 3

| | |
|--|-------------------------------|
| End point title | Pain at rest (PAR) at visit 3 |
| End point description: | |
| The patients' pain at rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h), V6 (96 h), V7 (120 h) and V8 (7 d) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question: "How would you describe your ankle pain right now?" "Wie würden Sie Ihre Schmerzen in Ihrem Sprunggelenk in diesem Moment beschreiben?" | |
| End point type | Secondary |
| End point timeframe: | |
| at visit 3 | |

| | | | | |
|--------------------------------------|-----------------|-----------------|--|--|
| End point values | Lixim patch | Placebo patch | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -8.5 (± 6.6) | -5.3 (± 8.7) | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0021 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.6395 |
| upper limit | -1.0432 |
| Variability estimate | Standard error of the mean |

Secondary: Pain at rest (PAR) at visit 4

| | |
|--|-------------------------------|
| End point title | Pain at rest (PAR) at visit 4 |
| End point description: | |
| The patients' pain at rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h), V6 (96 h), V7 (120 h) and V8 (7 d) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question: "How would you describe your ankle pain right now?" "Wie würden Sie Ihre Schmerzen in Ihrem Sprunggelenk in diesem Moment beschreiben?" | |
| End point type | Secondary |
| End point timeframe: | |
| at visit 4 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -13.2 (± 5.8) | -9.7 (± 6.1) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.1997 |
| upper limit | -2.0397 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
|----------------------|----------------------------|

Secondary: Pain at rest (PAR) at visit 5

| | |
|--|-------------------------------|
| End point title | Pain at rest (PAR) at visit 5 |
| End point description: | |
| The patients' pain at rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h), V6 (96 h), V7 (120 h) and V8 (7 d) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question: "How would you describe your ankle pain right now?" "Wie würden Sie Ihre Schmerzen in Ihrem Sprunggelenk in diesem Moment beschreiben?" | |
| End point type | Secondary |
| End point timeframe: | |
| at visit 5 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -15.0 (± 5.8) | -12.1 (± 5.4) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.1744 |
| upper limit | -1.6332 |
| Variability estimate | Standard error of the mean |

Secondary: Pain at rest (PAR) at visit 6

| | |
|---|-------------------------------|
| End point title | Pain at rest (PAR) at visit 6 |
| End point description: | |
| The patients' pain at rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h), V6 (96 h), V7 (120 h) and V8 (7 d) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question: "How would you describe your ankle pain right now?" | |

“Wie würden Sie Ihre Schmerzen in Ihrem Sprunggelenk in diesem Moment beschreiben?”

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| at visit 6 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -16.1 (± 5.5) | -13.8 (± 5.4) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.3337 |
| upper limit | -1.2672 |
| Variability estimate | Standard error of the mean |

Secondary: Pain at rest (PAR) at visit 7

| | |
|--|-------------------------------|
| End point title | Pain at rest (PAR) at visit 7 |
| End point description: | |
| The patients' pain at rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h), V6 (96 h), V7 (120 h) and V8 (7 d) using a 100 mm VAS from 0 = “no pain” to 100 = “extreme pain” in response to the question: “How would you describe your ankle pain right now?” “Wie würden Sie Ihre Schmerzen in Ihrem Sprunggelenk in diesem Moment beschreiben?” | |
| End point type | Secondary |
| End point timeframe: | |
| at visit 7 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -16.3 (\pm 5.7) | -14.7 (\pm 5.3) | | |

Statistical analyses

| Statistical analysis title | Treatment comparison - Test vs. placebo |
|---|---|
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0005 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6758 |
| upper limit | -0.4774 |
| Variability estimate | Standard error of the mean |

Secondary: Pain at rest (PAR) at visit 8

| | |
|---|-------------------------------|
| End point title | Pain at rest (PAR) at visit 8 |
| End point description: | |
| <p>The patients' pain at rest (PAR) was assessed at baseline, V2 (12 h), V3 (24 h), V4 (48 h), V5 (72 h), V6 (96 h), V7 (120 h) and V8 (7 d) using a 100 mm VAS from 0 = "no pain" to 100 = "extreme pain" in response to the question:</p> <p>"How would you describe your ankle pain right now?"</p> <p>"Wie würden Sie Ihre Schmerzen in Ihrem Sprunggelenk in diesem Moment beschreiben?"</p> | |
| End point type | Secondary |
| End point timeframe: | |
| at visit 8 | |

| End point values | Lixim patch | Placebo patch | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: mm | | | | |
| arithmetic mean (standard deviation) | -16.7 (\pm 5.3) | -15.9 (\pm 5.3) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0151 |
| Method | ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.5029 |
| upper limit | -0.05464 |
| Variability estimate | Standard error of the mean |

Secondary: Time to resolution of soft tissue injury/contusion

| | |
|------------------------|---|
| End point title | Time to resolution of soft tissue injury/contusion |
| End point description: | Resolution of soft tissue injury/contusion was assessed by the Investigator based on the patient's VAS ratings. |
| End point type | Secondary |
| End point timeframe: | Time of resolution was the time the point "0" (the left end) on the VAS was reached. |

| | | | | |
|--------------------------------------|-----------------|-----------------|--|--|
| End point values | Lixim patch | Placebo patch | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 55 | | |
| Units: hour | | | | |
| arithmetic mean (standard deviation) | 5.7 (± 1.6) | 8.5 (± 2.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Resolution of soft tissue injury/contusion responder at visit 8 (168h)

| | |
|------------------------|--|
| End point title | Resolution of soft tissue injury/contusion responder at visit 8 (168h) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | at visit 8 (168h) |

| | | | | |
|-----------------------------|-----------------|-----------------|--|--|
| End point values | Lixim patch | Placebo patch | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: YES | 119 | 36 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Global efficacy assessments by physician "very good" visit 4 (48hours))

| | |
|--|---|
| End point title | Global efficacy assessments by physician "very good" visit 4 (48hours)) |
| End point description: The investigator responded to the question: "Considering all the ways this treatment has affected the patient since he/she started in the study, how well is he/she doing?" The investigator's answer "0 = very good" is presented here. | |
| End point type | Secondary |
| End point timeframe: at visits 4 (48 h) | |

| | | | | |
|-----------------------------|-----------------|-----------------|--|--|
| End point values | Lixim patch | Placebo patch | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: percent | | | | |
| number (not applicable) | 62.50 | 16.67 | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Global efficacy assessments by physician "very good" visit 5 (72 hours)

| | |
|--|---|
| End point title | Global efficacy assessments by physician "very good" visit 5 (72 hours) |
| End point description: The investigator responded to the question: "Considering all the ways this treatment has affected the patient since he/she started in the study, how well is he/she doing?" The investigator's answer "0 = very good" is presented here. | |
| End point type | Secondary |
| End point timeframe: at visit 5 (72 hours) | |

| End point values | Lixim patch | Placebo patch | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: percent | | | | |
| number (not applicable) | 77.50 | 8.33 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Global efficacy assessments by physician "very good" visit 8 (168 hours)

| | |
|--|--|
| End point title | Global efficacy assessments by physician "very good" visit 8 (168 hours) |
| End point description: The investigator responded to the question: "Considering all the ways this treatment has affected the patient since he/she started in the study, how well is he/she doing?" The investigator's answer "0 = very good" is presented here. | |
| End point type | Secondary |

End point timeframe:
at visit 8 (168 hours)

| End point values | Lixim patch | Placebo patch | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: percent | | | | |
| number (not applicable) | 79.17 | 11.67 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Global efficacy assessments by patient "very good" at visit 4 (48 hours)

| | |
|------------------------|---|
| End point title | Global efficacy assessments by patient "very good" at visit 4 (48 hours) |
| End point description: | Percentage of patients, that responded "0 = very good" to the questions "Considering all the ways this treatment has affected you since you started in the study, how well are you doing?" is presented here. |
| End point type | Secondary |
| End point timeframe: | |
| at visit 4 (48 hours) | |

| End point values | Lixim patch | Placebo patch | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: percent | | | | |
| number (not applicable) | 49.17 | 8.33 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Global efficacy assessments by patient "very good" at visit 5 (72 hours)

| | |
|-----------------|--|
| End point title | Global efficacy assessments by patient "very good" at visit 5 (72 hours) |
|-----------------|--|

End point description:

Percentage of patients, that responded "0 = very good" to the questions "Considering all the ways this treatment has affected you since you started in the study, how well are you doing?" is presented here.

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

End point timeframe:

at visit 5 (72 hours)

| | | | | |
|-----------------------------|-----------------|-----------------|--|--|
| End point values | Lixim patch | Placebo patch | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: percent | | | | |
| number (not applicable) | 67.50 | 6.67 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Treatment comparison - Test vs. placebo |
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Cochran-Mantel-Haenszel |

Secondary: Global efficacy assessments by patient "very good" at visit 8 (168 hours)

| | |
|-----------------|---|
| End point title | Global efficacy assessments by patient "very good" at visit 8 (168 hours) |
|-----------------|---|

End point description:

Percentage of patients, that responded "0 = very good" to the questions "Considering all the ways this treatment has affected you since you started in the study, how well are you doing?" is presented here.

| | |
|------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| at visit 8 (168 hours) | |

| End point values | Lixim patch | Placebo patch | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 120 | 60 | | |
| Units: percent | | | | |
| number (not applicable) | 79.17 | 15.00 | | |

Statistical analyses

| Statistical analysis title | Treatment comparison - Test vs. placebo |
|---|---|
| Comparison groups | Lixim patch v Placebo patch |
| Number of subjects included in analysis | 180 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Cochran-Mantel-Haenszel |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall duration of study participation

Adverse event reporting additional description:

In general safety evaluations for this trial were performed for all patients who were randomised into the trial and received at least one dose of treatment.

Adverse Events are listed and evaluated descriptively with regard to frequency and intensity, relationship to the IMP, action taken, outcome, and seriousness as well as treatment group.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Lixim |
|-----------------------|-------|

Reporting group description: -

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

Reporting group description: -

| Serious adverse events | Lixim | Placebo | |
|---|-----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 120 (0.00%) | 0 / 60 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Lixim | Placebo | |
|---|-----------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 120 (1.67%) | 0 / 60 (0.00%) | |
| Injury, poisoning and procedural complications | | | |
| Joint injury | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | 0 / 60 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infections and infestations | | | |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | 0 / 60 (0.00%) | |
| occurrences (all) | 1 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

| |
|------|
| None |
|------|

Notes: