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

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)	
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)	1384.06180560 (± 239.18189325)	1469.67430560 (± 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)	2183.992361 10 (± 544.71997353)	2636.156944 40 (± 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)	2609.84930560 (± 780.32156579)	3614.43333330 (± 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)	2808.46145830 (± 927.63133296)	4375.905555560 (± 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)	2903.00868060 (± 1041.996621400)	4910.18333330 (± 1457.191196400)		

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)	-1192.807639000 (±	-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)	-2455.35069400 (±	-1373.96666700 (±		

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)	-3945.13854200 (±	-2275.294444000 (± 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)	-5538.99131900 (± 1023.0995730	-3403.81666700 (± 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 (± 5.7)	-14.7 (± 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:

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 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 (± 5.3)	-15.9 (± 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: