Clinical trial results:
Randomised, double-blind, placebo-controlled, parallel-groups, multi-centre clinical trial Phase III with Diclofenac Sodium 140 mg medicated plaster in patients with fresh impact injuries of the limbs.

Summary

EudraCT number	2010-020489-82
Trial protocol	DE
Global end of trial date	14 April 2011

Results information

Result version number	v1 (current)
This version publication date	16 July 2021
First version publication date	16 July 2021

Trial information

Trial identification

Sponsor protocol code	Q16-10-01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Fidia Farmaceutici S.p.A.
Sponsor organisation address	Via Ponte della Frabbrica 3/A, Abano Terme, Italy, 35031
Public contact	General Services, Fidia Farmaceutici S.p.A., 0039 0498232222, servizioportineria@fidiapharma.it
Scientific contact	Nicola Giordan, Head of Clinical Research, Fidia Farmaceutici S.p.A., 0039 0498232512, ngiordan@fidiapharma.it

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	25 July 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 April 2011
Global end of trial reached?	Yes
Global end of trial date	14 April 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial is to show superior efficacy of Diclofenac Sodium 140 mg medicated plaster over Placebo plaster as assessed by absolute change of pain on movement from baseline Visit 1 (Day 1) to Visit 3 (Day 3) in the indication fresh impact injuries of the limbs.

Protection of trial subjects:

Female patients who are not postmenopausal for at least 2 years or surgically sterilized and who are at risk of becoming pregnant must use a highly effective method of birth control. The contraceptive methods must be clearly stated in the patient documentation, and each of these women must have a negative pregnancy test before inclusion into the trial. The pregnancy tests has been provided by Fidia Farmaceutici S.p.A.
The investigator may withdraw the patient from the study at any time. Reasons for removing a patient from the trial include, but are not limited to:
- Adverse events
- Local intolerance of the plaster
- Unauthorised concomitant medication
- Major protocol violation that results in a significant risk to the patient's safety
- Unsatisfactory efficacy (defined as a worsening of pain on movement consisting in a difference on VAS scale of at least 19 mm from baseline Visit 135 to any other visit).
- Other reasons (e. g. randomisation code broken, pregnancy, etc.).
The patient should not take any concomitant treatment without the investigator's knowledge. All concomitant treatments/ therapies have to be recorded by the patient in the diary and then documented in the CRF by the investigator, giving INN, strength, galenic form, route of administration, dosage, date of start and end of treatment, and reason for therapy.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 September 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 168
Worldwide total number of subjects	168
EEA total number of subjects	168

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)	168
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Studied period:
September 2010 to April 2011 (7 months)
Date of first enrolment:
FPI: 14 September 2010
Date of last completed:
LPO: 14 April 2011
Study centres:
Four active centres in Germany

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	168
Number of subjects completed	168

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	Investigator, Monitor, Subject, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Diclofenac Sodium 140 mg medicated plaster

Arm description:

Diclofenac Sodium 140 mg medicated plaster, topical application in the morning and in the evening. Topical treatment is started after enrolment into the trial (following baseline measurement). The plaster is applied two times a day, approximately every 12 hours, in the morning and in the evening, continued for in total 7 days.

Arm type	Experimental
Investigational medicinal product name	Diclofenac Sodium 140 mg medicated plaster
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Topical use

Dosage and administration details:

140 mg Diclofenac Sodium medicated plaster, topical application, applied two times a day, approximately every 12 hours, in the morning and in the evening, continued for in total 7 days.

Arm title	Placebo plaster

Arm description:

Placebo plaster, topical application according to the dosage instruction for Diclofenac Sodium 140 mg medicated plaster.

Arm type	Placebo

Investigational medicinal product name	Placebo plaster
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Transdermal patch
Routes of administration	Topical use

Dosage and administration details:

Placebo plaster, topical treatment is started after enrolment into the trial (following baseline measurement). The plaster is applied two times a day, approximately every 12 hours, in the morning and in the evening, continued for in total 7 days.

Number of subjects in period 1	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster
Started	84	84
Completed	84	84

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	168	168	
Age categorical			
-Males or females, age range 18-60 years, outpatients. -Good general health. -Fresh impact injury of the limbs presented within 3 hours after injury. -The size of the visible traumatisation must be at least 25 cm2 and maximal 150 cm2 (in case of a muscle strain the area is assessed through palpation). -Pain assessment on movement by patient >=40 mm at baseline (Visit 1) on a 100 mm VAS.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	168	168	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	33.35		
standard deviation	± 11.25	-	
Gender categorical			
Units: Subjects			
Female	66	66	
Male	102	102	

Subject analysis sets

Subject analysis set title	Full analysis set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The full analysis set (FAS) will be defined as those patients who were randomised to one of the trial treatments (all randomised patients). In this trial population also patients with major protocol violations will be included.
The Full Analysis Set will be the primary population for the efficacy analyses in this superiority trial.

Subject analysis set title	Safety Set SAF
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety set comprises all patients of the full analysis set who received at least one dose of the investigational medical product.
This patient population will be used to analyse the safety data (e.g. AEs).

Subject analysis set title	Per-protocol set (PP)
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol set comprises all patients of the Full Analysis Set, who were treated with trial medication and who did not have any major protocol violations. Patients who terminated the trial prematurely due to inefficacy of the trial treatment and who did not have major protocol violations prior to trial termination will be included in the PP set.
The per-protocol set will be the secondary population for the efficacy analyses.

Reporting group values	Full analysis set	Safety Set SAF	Per-protocol set (PP)
Number of subjects	168	168	160
Age categorical			
-Males or females, age range 18-60 years, outpatients. -Good general health. -Fresh impact injury of the limbs presented within 3 hours after injury. -The size of the visible traumatisation must be at least 25 cm2 and maximal 150 cm2 (in case of a muscle strain the area is assessed through palpation). -Pain assessment on movement by patient >=40 mm at baseline (Visit 1) on a 100 mm VAS.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	168	168	160
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	33.35	33.35	33.27
standard deviation	± 11.25	± 11.25	± 11.20
Gender categorical			
Units: Subjects			
Female	66	66	62
Male	102	102	98

End points

End points reporting groups

Reporting group title	Diclofenac Sodium 140 mg medicated plaster

Reporting group description:

Diclofenac Sodium 140 mg medicated plaster, topical application in the morning and in the evening. Topical treatment is started after enrolment into the trial (following baseline measurement). The plaster is applied two times a day, approximately every 12 hours, in the morning and in the evening, continued for in total 7 days.

Reporting group title	Placebo plaster

Reporting group description:

Placebo plaster, topical application according to the dosage instruction for Diclofenac Sodium 140 mg medicated plaster.

Subject analysis set title	Full analysis set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The full analysis set (FAS) will be defined as those patients who were randomised to one of the trial treatments (all randomised patients). In this trial population also patients with major protocol violations will be included.
The Full Analysis Set will be the primary population for the efficacy analyses in this superiority trial.

Subject analysis set title	Safety Set SAF
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety set comprises all patients of the full analysis set who received at least one dose of the investigational medical product.
This patient population will be used to analyse the safety data (e.g. AEs).

Subject analysis set title	Per-protocol set (PP)
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol set comprises all patients of the Full Analysis Set, who were treated with trial medication and who did not have any major protocol violations. Patients who terminated the trial prematurely due to inefficacy of the trial treatment and who did not have major protocol violations prior to trial termination will be included in the PP set.
The per-protocol set will be the secondary population for the efficacy analyses.

Primary: Absolute change from baseline (Visit 1 (Day 1)) to Visit 3 (Day 3) regarding pain-on-movement VAS values

End point title	Absolute change from baseline (Visit 1 (Day 1)) to Visit 3 (Day 3) regarding pain-on-movement VAS values

End point description:

The primary efficacy variable was the absolute change from baseline (Visit 1 (Day 1)) to Visit 3 (Day 3) regarding pain-on-movement (POM) VAS values.

End point type	Primary

End point timeframe:

from baseline (Visit 1 (Day 1)) to Visit 3 (Day 3)

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster	Full analysis set	Per-protocol set (PP)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	84	84	168	160
Units: mm				
arithmetic mean (standard deviation)	-42.34 (± 20.69)	-18.09 (± 15.11)	-30.21 (± 21.77)	-30.47 (± 21.71)

Statistical analyses

Statistical analysis title	ANOVA
Statistical analysis description:	
The absolute changes from baseline to Visit 3, Visit 4, and Visit 5 were compared by means of analysis-of-variance (ANOVA)	
Comparison groups	Diclofenac Sodium 140 mg medicated plaster v Placebo plaster v Full analysis set v Per-protocol set (PP)
Number of subjects included in analysis	496
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.05
Method	ANOVA
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided

Secondary: Absolute change from baseline Visit 1 to Visit 4 in pain on movement assessed by patients using VAS.

End point title	Absolute change from baseline Visit 1 to Visit 4 in pain on movement assessed by patients using VAS.
End point description:	
End point type	Secondary
End point timeframe:	
from baseline Visit 1 to Visit 4 .	

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster	Full analysis set	Per-protocol set (PP)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	84	84	168	160
Units: mm				
arithmetic mean (standard deviation)	-59.36 (± 19.10)	-32.65 (± 19.34)	-46.01 (± 23.38)	-46.57 (± 23.03)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline Visit 1 to Visit 5 in pain on movement assessed by patients using VAS.

End point title	Absolute change from baseline Visit 1 to Visit 5 in pain on movement assessed by patients using VAS.

End point description:

End point type	Secondary

End point timeframe:

from baseline Visit 1 to Visit 5

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster	Full analysis set	Per-protocol set (PP)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	84	84	168	160
Units: mm				
arithmetic mean (standard deviation)	-71.79 (± 16.36)	-43.49 (± 19.13)	-57.64 (± 2272)	-58.60 (± 21.97)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline Visit 1 to Visit 3 in pain at rest assessed by patients using VAS.

End point title	Absolute change from baseline Visit 1 to Visit 3 in pain at rest assessed by patients using VAS.

End point description:

End point type	Secondary

End point timeframe:

from baseline Visit 1 to Visit 3

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster	Full analysis set	Per-protocol set (PP)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	84	84	168	160
Units: mm				
arithmetic mean (standard deviation)	-31.39 (± 18.82)	-20.74 (± 17.85)	-26.06 (± 19.05)	-26.49 (± 19.25)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline Visit 1 to Visit 4 in pain at rest assessed by patients using VAS.

End point title	Absolute change from baseline Visit 1 to Visit 4 in pain at rest assessed by patients using VAS.

End point description:

End point type	Secondary

End point timeframe:

from baseline Visit 1 to Visit 4

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster	Full analysis set	Per-protocol set (PP)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	84	84	168	160
Units: mm				
arithmetic mean (standard deviation)	-39.20 (± 18.58)	-27.19 (± 18.57)	-33.20 (± 19.47)	-33.80 (± 19.49)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute change from baseline Visit 1 to Visit 5 in pain at rest assessed by patients using VAS.

End point title	Absolute change from baseline Visit 1 to Visit 5 in pain at rest assessed by patients using VAS.

End point description:

End point type	Secondary

End point timeframe:

from baseline Visit 1 to Visit 5

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster	Full analysis set	Per-protocol set (PP)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	84	84	168	160
Units: mm				
arithmetic mean (standard deviation)	-43.17 (± 18.77)	-33.18 (± 17.34)	-38.17 (± 18.69)	-38.96 (± 18.52)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to onset of efficacy.

End point title	Time to onset of efficacy.

End point description:

End point type	Secondary

End point timeframe:

Time to onset of efficacy assessed by patient on Visit 2, possibly on Visit 3, 4 and 5, too. If the patient feels that the medication is not yet working at Visit 2, the investigator will ask the patient again at subsequent visits.

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	84		
Units: day				
arithmetic mean (standard error)	2.25000 (± 0.08102)	5.43037 (± 0.28324)		

Statistical analyses

No statistical analyses for this end point

Secondary: Global assessment of treatment efficacy by patient and investigator.

End point title	Global assessment of treatment efficacy by patient and investigator.

End point description:

Global assessment of treatment efficacy will be performed by patient and investigator at Visit 2, 3 and 4 (Day 2, 3 and 4) and the final visit (Visit 5) and is classified according the 5 point Likert scale

End point type	Secondary

End point timeframe:

at Visit 2, 3 and 4 (Day 2, 3 and 4) and the final visit (Visit 5)

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster	Full analysis set	Safety Set SAF
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	84	84	168	168
Units: likert scale	84	84	168	168

End point values	Per-protocol set (PP)			
Subject group type	Subject analysis set			
Number of subjects analysed	160			
Units: likert scale	160			

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of analgesic medication (paracetamol tablets).

End point title	Consumption of analgesic medication (paracetamol tablets).

End point description:

The consumption of rescue medication paracetamol (maximum dose per day (24 h) 2000 mg Paracetamol, single dose maximal 500-1000 mg equivalent to 10-15 mg/kg body weight) will be recorded in the diary by the patient and will then be documented in the CRF by the investigator.

End point type	Secondary

End point timeframe:

From baseline to visit 5 (Day 8).

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster	Full analysis set	Per-protocol set (PP)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	84	84	168	160
Units: Number of tablets	7	12	19	19

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to V3 regarding the tenderness of injured site VAS values

End point title	Change from Baseline to V3 regarding the tenderness of injured site VAS values

End point description:

End point type	Secondary

End point timeframe:

From Baseline (Day 1) to V3 (Day 3)

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster	Full analysis set	Per-protocol set (PP)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	84	84	168	160
Units: N/cm2				
arithmetic mean (standard deviation)	14.4048 (± 11.0269)	6.3214 (± 5.8023)	8.0833 (± 8.8108)	7.9562 (± 8.8274)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to V4 regarding the tenderness of injured site VAS values

End point title	Change from Baseline to V4 regarding the tenderness of injured site VAS values

End point description:

End point type	Secondary

End point timeframe:

From Baseline (Day 1) to V4 (Day 5)

End point values	Diclofenac Sodium 140 mg medicated plaster	Placebo plaster	Full analysis set	Per-protocol set (PP)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	84	84	168	160
Units: N/cm2				
arithmetic mean (standard deviation)	23.8452 (± 12.4567)	11.8214 (± 7.8788)	12.0238 (± 10.4222)	11.7888 (± 10.4913)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The AE assessment occurred at each visit at sites from V1 to V5. All AE occurred during the trial must be reported in the CRF. Any SAE occurring in a patient after providing informed consent and until 4 weeks after completion of the trial must be reported

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Safety Population SAF

Reporting group description:

All 168 patients enrolled who received at least one dose of the study medication were included in the safety population (SAF).

Adverse events (AEs) with multiple descriptions were splitted into single AEs for analysis purposes. Recurring AEs were counted only once. If there were differences in the corresponding AE assessments, the worst assessment was used.

Serious adverse events	Safety Population SAF		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 168 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0.1 %

Non-serious adverse events	Safety Population SAF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 168 (7.14%)		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 168 (0.60%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 168 (1.19%)		
occurrences (all)	2		
General disorders and administration site conditions			

Application site erythema, pruritus, dryness, pain subjects affected / exposed occurrences (all)	8 / 168 (4.76%) 10		
Infections and infestations Cystitis subjects affected / exposed occurrences (all)	1 / 168 (0.60%) 1		
Metabolism and nutrition disorders Hyperlipidaemia subjects affected / exposed occurrences (all)	1 / 168 (0.60%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported