Clinical trial results:
Randomized, Controlled, Double-blind, Placebo-controlled, Multi-center Hypothesis-finding Trial to Compare the Efficacy and Safety of a 10% Naproxen Gel vs. a 2.32% Diclofenac Diethylamine Gel and Placebo in the Treatment of Acute Soft Tissue Injuries of the Lower Extremities

Summary

EudraCT number	2020-004343-92
Trial protocol	DE
Global end of trial date	20 December 2021

Results information

Result version number	v1 (current)
This version publication date	29 December 2022
First version publication date	29 December 2022

Trial information

Trial identification

Sponsor protocol code	BAYH6689/21559

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05026320
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 December 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effectivenss of a naproxen topical gel 10%, diclofenac diethylamine 2.32% and placebo for relieving tenderness to pressure in subjects with acute soft tissue injuries of the lower extremities.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 August 2021
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: 76
Worldwide total number of subjects	76
EEA total number of subjects	76

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)	76
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in three centers in Germany. First subject first visit of the study was on 08 AUG 2021, and last subject last visit was on 20 DEC 2021.

Pre-assignment

Screening details:

Overall 76 subjects completed screening and were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Naproxen Topical Gel

Arm description:

Subjects received naproxen topical gel twice daily for 5 days.

Arm type	Experimental
Investigational medicinal product name	Naproxen Gel
Investigational medicinal product code	BAYH6689
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Twice a day (BID) for 5 days (final application on morning of Day 6)

Arm title	Diclofenac Diethylamine Topical Gel

Arm description:

Subjects received diclofenac diethylamine topical gel twice daily for 5 days.

Arm type	Active comparator
Investigational medicinal product name	Diclofenac Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Twice a day (BID) for 5 days (final application on morning of Day 6)

Arm title	Placebo

Arm description:

Subjects received placebo twice daily for 5 days.

Arm type	Placebo
Investigational medicinal product name	Placebo Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:
Twice a day (BID) for 5 days (final application on morning of Day 6)

Number of subjects in period 1	Naproxen Topical Gel	Diclofenac Diethylamine Topical Gel	Placebo
Started	31	30	15
Completed	31	30	15

Baseline characteristics

Reporting groups	
Reporting group title	Naproxen Topical Gel
Reporting group description:	
Subjects received naproxen topical gel twice daily for 5 days.	
Reporting group title	Diclofenac Diethylamine Topical Gel
Reporting group description:	
Subjects received diclofenac diethylamine topical gel twice daily for 5 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo twice daily for 5 days.	

Reporting group values	Naproxen Topical Gel	Diclofenac Diethylamine Topical Gel	Placebo
Number of subjects	31	30	15
Age Categorical			
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)	31	30	15
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	33.32	31.57	32.47
standard deviation	± 10.74	± 9.47	± 13.05
Gender Categorical			
Units: Subjects			
Female	16	16	9
Male	15	14	6

Reporting group values	Total		
Number of subjects	76		
Age Categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	76		
From 65-84 years	0		
85 years and over	0		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	41		
Male	35		

End points

End points reporting groups

Reporting group title	Naproxen Topical Gel
Reporting group description:	
Subjects received naproxen topical gel twice daily for 5 days.	
Reporting group title	Diclofenac Diethylamine Topical Gel
Reporting group description:	
Subjects received diclofenac diethylamine topical gel twice daily for 5 days.	
Reporting group title	Placebo
Reporting group description:	
Subjects received placebo twice daily for 5 days.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety population included all randomized patients who received at least one dose of the study treatment.	
Subject analysis set title	Intent to treat (ITT)/Full Analysis Set (FAS)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects who were randomized and provided at least one measure of primary efficacy parameter after the first application of the study treatment.	
Subject analysis set title	Per protocol population (PP)
Subject analysis set type	Per protocol
Subject analysis set description:	
The Per Protocol population included all subjects in Intent to treat (ITT) who completed the study and did not have any major protocol violations.	

Primary: Tenderness (algometry) over the initial 72 hours

End point title	Tenderness (algometry) over the initial 72 hours
End point description:	
Algometry area under the curve (AUC) from zero to 72h post dose	
End point type	Primary
End point timeframe:	
Up to 72 hours post dose	

End point values	Naproxen Topical Gel	Diclofenac Diethylamine Topical Gel	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30[1]	28[2]	14[3]	
Units: Nxh/cm^2				
arithmetic mean (standard deviation)	1213.88 (± 461.11)	1041.04 (± 274.25)	850.79 (± 276.04)	

Notes:

[1] - Per protocol population

[2] - Per protocol population

[3] - Per protocol population

Statistical analyses

Statistical analysis title	Analysis of Covariance (ANCOVA)
Comparison groups	Naproxen Topical Gel v Diclofenac Diethylamine Topical Gel v Placebo
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0221
Method	ANCOVA

Secondary: Percentage of subjects with at least one treatment emergent adverse event after treatment

End point title	Percentage of subjects with at least one treatment emergent adverse event after treatment

End point description:

An AE is any untoward medical occurrence in a clinical study participant, associated with the use of study intervention, whether or not considered related to the study intervention.

End point type	Secondary

End point timeframe:

After first treatment on Day 1 until follow-up visit (Day 30)

End point values	Naproxen Topical Gel	Diclofenac Diethylamine Topical Gel	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[4]	30[5]	15[6]	
Units: percentage (%)				
number (not applicable)				
any AE	0	3.33	0	
serious AE	0	0	0	

Notes:

[4] - Safety population

[5] - Safety population

[6] - Safety population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with at least one treatment emergent adverse event after treatment

End point title	Number of subjects with at least one treatment emergent adverse event after treatment

End point description:

An AE is any untoward medical occurrence in a clinical study participant, associated with the use of study intervention, whether or not considered related to the study intervention.

End point type	Secondary

End point timeframe:

After first treatment on Day 1 until follow-up visit (Day 30)

End point values	Naproxen Topical Gel	Diclofenac Diethylamine Topical Gel	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31[7]	30[8]	15[9]	
Units: participants				
Rhinitis	0	1	0	
Nasal congestion	0	1	0	
Paranasal sinus hypersecretion	0	1	0	

Notes:

[7] - Safety population

[8] - Safety population

[9] - Safety population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse event data were collected after first treatment on Day 1 until follow-up visit (Day 30).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	Naxopren Gel
Reporting group description:	
Participants received Naxopren topical gel (BAYH006689) two times a day (bid) for 5 days.	
Reporting group title	Placebo Gel
Reporting group description:	
Participants received Placebo gel bid for 5 days.	
Reporting group title	Diclofenac Gel
Reporting group description:	
Participants received Diclofenac Diethylamine gel bid for 5 days.	

Serious adverse events	Naxopren Gel	Placebo Gel	Diclofenac Gel
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)	0 / 15 (0.00%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Naxopren Gel	Placebo Gel	Diclofenac Gel
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
Respiratory, thoracic and mediastinal disorders			
Paranasal sinus hypersecret			
subjects affected / exposed	0 / 31 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 31 (0.00%)	0 / 15 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Infections and infestations			

Rhinitis subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	0 / 15 (0.00%) 0	1 / 30 (3.33%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 November 2021	Amendment 3 specified following modifications: Exclusion Criteria, Statistical Hypotheses, Sample Size Determination, Analysis Sets – Per Protocol, Statistical Analysis

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported