Clinical trial results:
A Double-Blind, Randomized, Dose Selection Vehicle–Controlled Multicenter Clinical Study for Evaluation of the Safety, Tolerability, Efficacy, and Pharmacokinetics of topical Neramexane in Subjects with Moderate to Severe Acne

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines

Summary

EudraCT number	2011-004998-83
Trial protocol	DE
Global end of trial date	19 August 2013

Results information

Result version number	v1 (current)
This version publication date	29 December 2016
First version publication date	29 December 2016

Trial information

Trial identification

Sponsor protocol code	MUS92579_2057_1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Merz Pharmaceuticals GmbH
Sponsor organisation address	Eckenheimer Landstr. 100, Frankfurt, Germany, 60318
Public contact	Public Disclosure Manager, Merz Pharmaceuticals GmbH, +49 69 1503 0, clinicaltrials@merz.de
Scientific contact	Public Disclosure Manager, Merz Pharmaceuticals GmbH, +49 69 1503 0, clinicaltrials@merz.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	09 July 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety, tolerability, efficacy and pharmacokinetics of three concentrations [0.5 percent (%), 1.5 % and 3 %] of topical anti-Acne product Neramexane mesylate gel, quaque die (qd) when compared to vehicle in subjects with Moderate to Severe Acne.

Protection of trial subjects:

High medical and ethical standards were followed in accordance with Good Clinical Practice and other applicable regulations. In addition, an independent data monitoring committee was in charge of monitoring subject safety while the study was ongoing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 April 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 237
Worldwide total number of subjects	237
EEA total number of subjects	237

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)	84
Adults (18-64 years)	153
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 292 subjects were screened for eligibility. 55 of these subjects were screening failures, the remaining 237 subjects were eligible to be randomized and applied investigational product.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Vehicle

Arm description:

Vehicle 0.5 g topical gel

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

Dosage and administration details:

Subjects received vehicle 0.5 gram (g) topical gel on every morning during Stage 1 and on every evening after removal of makeup before going to sleep during Stage 2. The total duration of treatment was 12 Weeks.

Arm title	Neramexane mesylate 0.5 Percent (%)

Arm description:

0.5% Neramexane mesylate 0.5 g topical gel

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

Dosage and administration details:

Subjects received 0.5% Neramexane mesylate 0.5 g topical gel on every morning during Stage 1 and on every evening after removal of makeup before going to sleep during Stage 2. The total duration of treatment was 12 Weeks.

Arm title	Neramexane mesylate 1.5%

Arm description:

1.5% Neramexane mesylate 0.5 g topical gel

Arm type	Experimental

Investigational medicinal product name	Neramexane mesylate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Subjects received 1.5% Neramexane mesylate 0.5 g topical gel on every morning during Stage 1 and on every evening after removal of makeup before going to sleep during Stage 2. The total duration of treatment was 12 Weeks.

Arm title	Neramexane mesylate 3%

Arm description:

3% Neramexane mesylate 0.5 g topical gel

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

Dosage and administration details:

Subjects received 3% Neramexane mesylate 0.5 g topical gel on every morning during Stage 1 and on every evening after removal of makeup before going to sleep during Stage 2. The total duration of treatment was 12 Weeks.

Number of subjects in period 1	Vehicle	Neramexane mesylate 0.5 Percent (%)	Neramexane mesylate 1.5%
Started	59	59	59
Completed	51	49	45
Not completed	8	10	14
Consent withdrawn by subject	-	2	3
Adverse event, non-fatal	2	-	-
Administrative reasons	6	8	11
Protocol deviation	-	-	-

Number of subjects in period 1	Neramexane mesylate 3%
Started	60
Completed	49
Not completed	11
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Administrative reasons	7
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Vehicle
Reporting group description:	
Vehicle 0.5 g topical gel	
Reporting group title	Neramexane mesylate 0.5 Percent (%)
Reporting group description:	
0.5% Neramexane mesylate 0.5 g topical gel	
Reporting group title	Neramexane mesylate 1.5%
Reporting group description:	
1.5% Neramexane mesylate 0.5 g topical gel	
Reporting group title	Neramexane mesylate 3%
Reporting group description:	
3% Neramexane mesylate 0.5 g topical gel	

Reporting group values	Vehicle	Neramexane mesylate 0.5 Percent (%)	Neramexane mesylate 1.5%
Number of subjects	59	59	59
Age categorical Units: Subjects			
Adolescents (12-17 years)	16	27	24
Adults (18-64 years)	43	32	35
Gender categorical Units: Subjects			
Female	31	24	21
Male	28	35	38

Reporting group values	Neramexane mesylate 3%	Total	
Number of subjects	60	237	
Age categorical Units: Subjects			
Adolescents (12-17 years)	18	85	
Adults (18-64 years)	42	152	
Gender categorical Units: Subjects			
Female	30	106	
Male	30	131	

End points

End points reporting groups	
Reporting group title	Vehicle
Reporting group description: Vehicle 0.5 g topical gel	
Reporting group title	Neramexane mesylate 0.5 Percent (%)
Reporting group description: 0.5% Neramexane mesylate 0.5 g topical gel	
Reporting group title	Neramexane mesylate 1.5%
Reporting group description: 1.5% Neramexane mesylate 0.5 g topical gel	
Reporting group title	Neramexane mesylate 3%
Reporting group description: 3% Neramexane mesylate 0.5 g topical gel	

Primary: Change From Baseline in Inflammatory Acne Lesion Counts at Week 12	
End point title	Change From Baseline in Inflammatory Acne Lesion Counts at Week 12
End point description: The inflammatory acne lesions were counted. In the counting procedure, primary acne lesions were evaluated and accounted independently for papules and pustules, and nodules greater than or equal to 5 millimeters (mm) in diameter. The nose region was included in the counting only for inflammatory lesions. The full analysis set (FAS) was the subset of subjects in the safety evaluation set (SES), all subjects who had the baseline and at least one post-baseline value of the primary efficacy variable. The Multiple Imputation (MI) missing value imputation method was used.	
End point type	Primary
End point timeframe: Baseline and Week 12	

End point values	Vehicle	Neramexane mesylate 0.5 Percent (%)	Neramexane mesylate 1.5%	Neramexane mesylate 3%
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	52	52	52
Units: lesion				
arithmetic mean (standard deviation)				
Baseline	29.5 (± 9)	32.4 (± 10.1)	31 (± 8.4)	30.5 (± 8.6)
Change at Week 12	-10.5 (± 11.7)	-10.9 (± 10.9)	-9.7 (± 9.4)	-10.9 (± 12.8)

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Vehicle v Neramexane mesylate 0.5 Percent (%)

Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7972
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	4.8

Statistical analysis title	Statistical Analysis 2
Comparison groups	Vehicle v Neramexane mesylate 1.5%
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5228
Method	ANCOVA
Parameter estimate	Least Square Mean Difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	5.5

Statistical analysis title	Statistical Analysis 3
Comparison groups	Vehicle v Neramexane mesylate 3%
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9677
Method	ANCOVA
Parameter estimate	Least Square Mean Differences
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	4.2

Secondary: Change From Baseline in Non-Inflammatory Acne Lesion Counts at Week

12

End point title	Change From Baseline in Non-Inflammatory Acne Lesion Counts at Week 12

End point description:

The non-inflammatory acne lesions were counted. In the counting procedure, primary acne lesions were evaluated and accounted independently for open and closed comedones. The nose region was excluded in the counting for non-inflammatory lesions. The FAS was the subset of subjects in the SES, all subjects who had the baseline and at least one post-baseline value of the primary efficacy variable. The MI missing value imputation method was used.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	Vehicle	Neramexane mesylate 0.5 Percent (%)	Neramexane mesylate 1.5%	Neramexane mesylate 3%
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	52	52	52
Units: lesion				
arithmetic mean (standard deviation)				
Baseline	43.4 (± 19.1)	45.6 (± 20.5)	45.3 (± 22.5)	49.4 (± 22)
Change at Week 12	-6.7 (± 23.3)	-9.2 (± 19.3)	-8.4 (± 21.1)	-9.5 (± 19.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Two Grade Improvement in Evaluator Global Severity Score (EGSS) at Week 12

End point title	Number of Subjects With Two Grade Improvement in Evaluator Global Severity Score (EGSS) at Week 12

End point description:

The EGSS was performed to assess the grade of the acne. The grading ranges from 0 to 5. Clear (0): Normal, clear skin with no evidence of acne vulgaris; Almost Clear (1): Rare non-inflammatory lesions present, with rare non-inflamed papules; Mild (2): Some non-inflammatory lesions are present, with few inflammatory lesions; Moderate (3): Non-inflammatory lesions predominating, with multiple inflammatory lesions evident and several to many comedones and papules/pustules, there may be one small nodulocystic lesion; Severe (4): Inflammatory lesions more apparent, with many comedones and papules/pustules, there may be a few nodulocystic lesions; Very Severe (5): Highly inflammatory lesions predominating, with variable numbers of comedones, many papules/pustules, and many nodulocystic lesions. The FAS was the subset of subjects in the SES, all subjects who had the baseline and at least one post-baseline.

End point type	Secondary

End point timeframe:

Week 12

End point values	Vehicle	Neramexane mesylate 0.5 Percent (%)	Neramexane mesylate 1.5%	Neramexane mesylate 3%
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	52	52	52
Units: subject	4	6	4	4

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Screening (Week -2) until Safety Follow-up (Up to Week 14)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups	
Reporting group title	Vehicle
Reporting group description:	
Subjects received vehicle 0.5 gram (g) topical gel on every morning during Stage 1 and on every evening after removal of makeup before going to sleep during Stage 2. The total duration of treatment was 12 Weeks.	
Reporting group title	Neramexane mesylate 0.5 Percent (%)
Reporting group description:	
Subjects received 0.5% Neramexane mesylate 0.5 g topical gel on every morning during Stage 1 and on every evening after removal of makeup before going to sleep during Stage 2. The total duration of treatment was 12 Weeks.	
Reporting group title	Neramexane mesylate 1.5%
Reporting group description:	
Subjects received 1.5% Neramexane mesylate 0.5 g topical gel on every morning during Stage 1 and on every evening after removal of makeup before going to sleep during Stage 2. The total duration of treatment was 12 Weeks.	
Reporting group title	Neramexane mesylate 3%
Reporting group description:	
Subjects received 3% Neramexane mesylate 0.5 g topical gel on every morning during Stage 1 and on every evening after removal of makeup before going to sleep during Stage 2. The total duration of treatment was 12 Weeks.	

Serious adverse events	Vehicle	Neramexane mesylate 0.5 Percent (%)	Neramexane mesylate 1.5%
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	1 / 59 (1.69%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 59 (0.00%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Intestinal adhesion lysis			

subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Neramexane mesylate 3%		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Joint dislocation			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Intestinal adhesion lysis			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Vehicle	Neramexane mesylate 0.5 Percent (%)	Neramexane mesylate 1.5%
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 59 (49.15%)	29 / 59 (49.15%)	40 / 59 (67.80%)
Surgical and medical procedures			
Wisdom teeth removal			
subjects affected / exposed	3 / 59 (5.08%)	0 / 59 (0.00%)	2 / 59 (3.39%)
occurrences (all)	3	0	3
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 59 (6.78%)	6 / 59 (10.17%)	6 / 59 (10.17%)
occurrences (all)	7	6	10
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	3 / 59 (5.08%)	9 / 59 (15.25%)	20 / 59 (33.90%)
occurrences (all)	3	18	32
Application site pruritus			
subjects affected / exposed	6 / 59 (10.17%)	4 / 59 (6.78%)	16 / 59 (27.12%)
occurrences (all)	6	6	31
Application site dryness			
subjects affected / exposed	5 / 59 (8.47%)	10 / 59 (16.95%)	8 / 59 (13.56%)
occurrences (all)	9	15	13
Application site exfoliation			
subjects affected / exposed	3 / 59 (5.08%)	7 / 59 (11.86%)	4 / 59 (6.78%)
occurrences (all)	3	7	4
Application site erythema			
subjects affected / exposed	3 / 59 (5.08%)	1 / 59 (1.69%)	2 / 59 (3.39%)
occurrences (all)	3	1	2
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 59 (3.39%)	3 / 59 (5.08%)	2 / 59 (3.39%)
occurrences (all)	2	3	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	13 / 59 (22.03%)	11 / 59 (18.64%)	21 / 59 (35.59%)
occurrences (all)	13	15	22
Oral herpes			

subjects affected / exposed	3 / 59 (5.08%)	1 / 59 (1.69%)	1 / 59 (1.69%)
occurrences (all)	3	1	2

Non-serious adverse events	Neramexane mesylate 3%		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 60 (61.67%)		
Surgical and medical procedures			
Wisdom teeth removal			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
General disorders and administration site conditions			
Application site pain			
subjects affected / exposed	23 / 60 (38.33%)		
occurrences (all)	28		
Application site pruritus			
subjects affected / exposed	12 / 60 (20.00%)		
occurrences (all)	19		
Application site dryness			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	6		
Application site exfoliation			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	4		
Application site erythema			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	21 / 60 (35.00%) 22		
Oral herpes subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 March 2012	Amendment prior to study start to address comments by BfArM and Ethics Committee.
11 May 2012	Main reason for the amendment was to address practical issues observed during treatment of the first study subjects, including a dose reduction to 0.5 gram (g) of gel daily.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported