Clinical trial results:
Patient-Reported Outcomes of Brimonidine Tartrate 0.5% Gel for Treatment of Severe Facial Erythema of Rosacea

Summary

EudraCT number	2012-005686-12
Trial protocol	GB SE DE
Global end of trial date	14 November 2013

Results information

Result version number	v1 (current)
This version publication date	22 October 2020
First version publication date	22 October 2020
Summary attachment (see zip file)	2012-005686-12 (Summary Attachment.pdf)

Trial information

Trial identification

Sponsor protocol code	RD.03.SPR.29107

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01885000
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galderma R&D
Sponsor organisation address	2400 route des colles, Biot, France, 06410
Public contact	CTA Coordinator, Galderma R&D, 33 (0)493 95 70 85, cta.coordinator@galderma.com
Scientific contact	CTA Coordinator, Galderma R&D, 33 (0)493 95 70 85, cta.coordinator@galderma.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	14 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 November 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 subject-reported outcomes following the treatment of severe facial erythema of rosacea with brimonidine tartrate 0.5 percent (%) gel compared with vehicle gel. The safety and efficacy of the two treatment regimens were also evaluated.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2013
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	Sweden: 10
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Germany: 56
Worldwide total number of subjects	92
EEA total number of subjects	92

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)	71

From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

No screening

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, Data analyst, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Brimonidine Tartrate 0.5% gel

Arm description:

Subjects applied brimonidine tartrate 0.5% gel topically once daily for 8 days.

Arm type	Experimental
Investigational medicinal product name	Brimonidine tartrate
Investigational medicinal product code	
Other name	Mirvaso
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Brimonidine tartrate was applied cutaneously once daily for 8 days.

Arm title	Vehicle

Arm description:

Subjects applied brimonidine tartrate vehicle gel topically once daily for 8 days.

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

Dosage and administration details:

Brimonidine tartrate vehicle was applied cutaneously once daily for 8 days.

Number of subjects in period 1	Brimonidine Tartrate 0.5% gel	Vehicle
Started	48	44
Completed	46	42
Not completed	2	2
Consent withdrawn by subject	1	1
Adverse event, non-fatal	1	-

Protocol violation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Brimonidine Tartrate 0.5% gel
Reporting group description:	
Subjects applied brimonidine tartrate 0.5% gel topically once daily for 8 days.	
Reporting group title	Vehicle
Reporting group description:	
Subjects applied brimonidine tartrate vehicle gel topically once daily for 8 days.	

Reporting group values	Brimonidine Tartrate 0.5% gel	Vehicle	Total
Number of subjects	48	44	92
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)	37	34	71
From 65-84 years	11	10	21
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	53.4	54.9	
standard deviation	± 12.9	± 12.8	-
Gender categorical Units: Subjects			
Female	30	26	56
Male	18	18	36
Race Units: Subjects			
White	48	44	92
Skin phototype Units: Subjects			
Type I	3	6	9
Type II	34	27	61
Type III	11	11	22

End points

End points reporting groups

Reporting group title	Brimonidine Tartrate 0.5% gel
Reporting group description:	
Subjects applied brimonidine tartrate 0.5% gel topically once daily for 8 days.	
Reporting group title	Vehicle
Reporting group description:	
Subjects applied brimonidine tartrate vehicle gel topically once daily for 8 days.	

Primary: Percentage of Subjects who are Very satisfied/satisfied/somewhat satisfied with the Overall Study Treatment

End point title	Percentage of Subjects who are Very satisfied/satisfied/somewhat satisfied with the Overall Study Treatment
End point description:	
Percentage of subjects who are very satisfied/satisfied/somewhat satisfied with the study treatment were reported. Intent-to-Treat (ITT) population consisted of the entire population enrolled and randomized. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point.	
End point type	Primary
End point timeframe:	
Day 8	

End point values	Brimonidine Tartrate 0.5% gel	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	42		
Units: Percentage of subjects				
number (not applicable)	69.6	40.4		

Statistical analyses

Statistical analysis title	Brimonidine Tartrate 0.5% gel versus Vehicle
Comparison groups	Brimonidine Tartrate 0.5% gel v Vehicle
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0065
Method	Cochran-Mantel-Haenszel

Primary: EuroQuality of Life-5 Dimensional-3 Level (EQ-5D-3L) Questionnaire at Day

8

End point title	EuroQuality of Life-5 Dimensional-3 Level (EQ-5D-3L) Questionnaire at Day 8

End point description:

EQ-5D-3L questionnaire validated questionnaire addressed 5 questions on 1. mobility, 2.self-care, 3.usual activities, 4.pain/discomfort and 5. anxiety/depression. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point.

End point type	Primary

End point timeframe:

Day 8

End point values	Brimonidine Tartrate 0.5% gel	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	42		
Units: Percentage of subjects				
number (not applicable)				
1. I have no problems in walking about	95.7	92.9		
1.I have some problems in walking about	4.3	7.1		
2. I have no problems with self-care	97.8	97.6		
2. I have some problems washing or dressing myself	2.2	2.4		
3.I have no problems with performing usualactivity	91.3	90.5		
3.I have some problems withperformingusualactivity	8.7	9.5		
4.I have no pain or discomfort	58.7	76.2		
4.I have moderate pain or discomfort	41.3	21.4		
4.I have extreme pain or discomfort	0	2.4		
5.I am not anxious or depressed	87.0	73.8		
5.I am moderately anxious or depressed	10.9	26.2		
5.I am extremely anxious or depressed	2.2	0		

Statistical analyses

Statistical analysis title	Mobility
Comparison groups	Vehicle v Brimonidine Tartrate 0.5% gel
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5821
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Self-Care

Comparison groups	Brimonidine Tartrate 0.5% gel v Vehicle
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8864
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Usual Activities
Comparison groups	Brimonidine Tartrate 0.5% gel v Vehicle
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9579
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Pain/Discomfort
Comparison groups	Brimonidine Tartrate 0.5% gel v Vehicle
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1344
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Anxiety/Depression
Comparison groups	Vehicle v Brimonidine Tartrate 0.5% gel
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1881
Method	Cochran-Mantel-Haenszel

Primary: Percent Change from Baseline in Total Score of Dermatology Life Quality Index (DLQI) Questionnaire at Day 8

End point title	Percent Change from Baseline in Total Score of Dermatology Life Quality Index (DLQI) Questionnaire at Day 8

End point description:

DLQI is a compact health-related quality of life index that has 10 questions and depends on the patients' self-declaration about experiences during the previous week. DLQI results range between grades 0 and 30. [Grade 0-1]: No effect at all on subject's life, [Grade 2-5]: Small effect at all on subject's life, [Grade 6-10]: Moderate effect at all on subject's life, [Grade 11-20]: Very large effect at all on subject's life, [Grade 21-30]: Extremely large effect at all on subject's life. As the DLQI scores increase, the impact of the studied disease on life becomes greater. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point.

End point type	Primary
End point timeframe: Baseline and Day 8	

End point values	Brimonidine Tartrate 0.5% gel	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	41		
Units: Score on scale				
arithmetic mean (standard deviation)	-15.4 (± 61.7)	-32.6 (± 43.7)		

Statistical analyses

Statistical analysis title	% change from Baseline in Total Score
Comparison groups	Brimonidine Tartrate 0.5% gel v Vehicle
Number of subjects included in analysis	86
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3935
Method	Cochran-Mantel-Haenszel

Primary: EuroQuality of Life-5 Dimensional-3 Level (EQ-5D-3L) Questionnaire (Along with a Visual Analogue Score for the Overall Health State) at Day 8

End point title	EuroQuality of Life-5 Dimensional-3 Level (EQ-5D-3L) Questionnaire (Along with a Visual Analogue Score for the Overall Health State) at Day 8

End point description:

EQ-5D-3L questionnaire validated questionnaire (along with a visual analogue score for the overall health state) was reported. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point.

End point type	Primary
End point timeframe: Day 8	

End point values	Brimonidine Tartrate 0.5% gel	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	42		
Units: Score on scale				
arithmetic mean (standard deviation)	76.0 (± 19.3)	80.2 (± 13.1)		

Statistical analyses

Statistical analysis title	EQ-5D-3L: Health State Today
Comparison groups	Brimonidine Tartrate 0.5% gel v Vehicle
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4162
Method	Cochran-Mantel-Haenszel

Secondary: Percentage of Subjects With at Least two Grade Improvement in the Clinician's Erythema Assessment (CEA)

End point title	Percentage of Subjects With at Least two Grade Improvement in the Clinician's Erythema Assessment (CEA)

End point description:

Percentage of subjects with at least one grade improvement in the CEA was reported. Evaluation of erythema by using CEA was assessed by 0 to 4 grades, where 0-Clear skin with no signs of erythema, 1-Almost clear; slight redness, 2-Mild erythema; definite redness, 3-Moderate erythema; marked redness, 4-Severe erythema; fiery redness. ITT population consisted of the entire population enrolled and randomized. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Day 8

End point values	Brimonidine Tartrate 0.5% gel	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	42		
Units: Percentage of subjects				
number (not applicable)	47.8	7.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With at Least two Grade Improvement in the Patient Self-assessment

End point title	Percentage of Subjects With at Least two Grade Improvement

	in the Patient Self-assessment

End point description:

Percentage of subjects with at least two grade improvement in the PSA was reported. Evaluation of erythema severity by using the PSA grades (0-4): 0- No redness, 1- very mild redness, 2-mild redness, 3-moderate redness, 4-severe redness. ITT population consisted of the entire population enrolled and randomized. Here 'N' number of subjects anlaysed signifies number of subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Day 8

End point values	Brimonidine Tartrate 0.5% gel	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	42		
Units: percentage of subjects				
number (not applicable)	41.3	23.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Facial inflammatory lesion counts at Day 8

End point title	Change from Baseline in Facial inflammatory lesion counts at Day 8

End point description:

Facial inflammatory lesions of rosacea (including papules and pustules) were counted by evaluator. Here 'n' number of subjects anlaysed signifies number of subjects evaluable for this end point.

End point type	Secondary

End point timeframe:

Day 8

End point values	Brimonidine Tartrate 0.5% gel	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	42		
Units: number of lesions				
arithmetic mean (standard deviation)	0.3 (± 2.5)	0.4 (± 1.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reported Adverse Events

End point title	Number of Subjects Reported Adverse Events

End point description:

Number of subjects with AE’s were reported. All Patient Treated (APT) population included all subjects enrolled in the study who had received the study treatment at least once.

End point type	Secondary

End point timeframe:

From start of study drug administration up to Day 8

End point values	Brimonidine Tartrate 0.5% gel	Vehicle		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	44		
Units: count of subjects	15	9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of study drug administration up to Day 8	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	15
Reporting groups	
Reporting group title	Brimonidine Tartrate 0.5% gel
Reporting group description: -	
Reporting group title	Vehicle
Reporting group description:	
Subjects applied brimonidine tartrate vehicle gel topically once daily for 8 days.	

Serious adverse events	Brimonidine Tartrate 0.5% gel	Vehicle	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	0 / 44 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Brimonidine Tartrate 0.5% gel	Vehicle	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 48 (31.25%)	9 / 44 (20.45%)	
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 48 (4.17%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 48 (2.08%)	2 / 44 (4.55%)	
occurrences (all)	1	2	
Hypoesthesia			

subjects affected / exposed	0 / 48 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 48 (2.08%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	6 / 48 (12.50%)	2 / 44 (4.55%)	
occurrences (all)	6	2	
Pain of skin			
subjects affected / exposed	1 / 48 (2.08%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 48 (2.08%)	1 / 44 (2.27%)	
occurrences (all)	1	1	
Skin burning sensation			
subjects affected / exposed	0 / 48 (0.00%)	2 / 44 (4.55%)	
occurrences (all)	0	2	
Rosacea			
subjects affected / exposed	2 / 48 (4.17%)	1 / 44 (2.27%)	
occurrences (all)	2	1	
Skin irritation			
subjects affected / exposed	0 / 48 (0.00%)	1 / 44 (2.27%)	
occurrences (all)	0	1	
Skin tightness			
subjects affected / exposed	4 / 48 (8.33%)	2 / 44 (4.55%)	
occurrences (all)	5	3	
Skin warm			
subjects affected / exposed	2 / 48 (4.17%)	1 / 44 (2.27%)	
occurrences (all)	9	2	
Swelling face			
subjects affected / exposed	1 / 48 (2.08%)	0 / 44 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Rash pustular			
subjects affected / exposed	2 / 48 (4.17%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 44 (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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26416154