Clinical trial results:
Evaluation of Acne-Induced Hyperpigmentation During Treatment of Acne Vulgaris Subjects With Trifarotene 50 µg/g Cream Versus Vehicle Cream Over 24 Weeks

Summary

EudraCT number	2021-003608-41
Trial protocol	ES
Global end of trial date	15 December 2022

Results information

Result version number	v1 (current)
This version publication date	24 December 2023
First version publication date	24 December 2023

Trial information

Trial identification

Sponsor protocol code	RD.06.SPR.204245

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05089708
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galderma S.A.
Sponsor organisation address	Avenue Gratta-Paille 2, Lausanne, Switzerland, 1018
Public contact	Clinical Trial Information Desk, Galderma S.A., ctacoordinator@galderma.com
Scientific contact	Clinical Trial Information Desk, Galderma S.A., ctacoordinator@galderma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001492-PIP01-13
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Main objective is to evaluate the efficacy and safety of trifarotene 50 microgram per gram (µg/g) cream compared to its vehicle cream in the treatment of moderate acne vulgaris with acne-induced postinflammatory hyperpigmentation (PIH) in subjects with Fitzpatrick Skin Types (FST) I-VI.

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice (GCP) as required by the International Conference for Harmonisation (ICH) guidelines. Compliance with these requirements also constitutes conformity with the ethical principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	22 December 2021
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	Spain: 9
Country: Number of subjects enrolled	United States: 114
Worldwide total number of subjects	123
EEA total number of subjects	9

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)	33
Adults (18-64 years)	90
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 18 investigational centers in United States and Spain from 22 Dec 2021 to 15 Dec 2022.

Pre-assignment

Screening details:

A total of 123 subjects were randomized and enrolled in two treatment groups. 60 subjects in Trifarotene (CD5789) Cream treatment group and 63 subjects in Trifarotene Vehicle Cream treatment group.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Trifarotene Cream

Arm description:

Subjects applied Trifarotene 50 (mcg/g) cream on face once daily in the evening for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Trifarotene
Investigational medicinal product code	CD5789
Other name	Aklief
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

Subjects applied a thin layer of trifarotene 50 mcg/g cream on the face once daily, in the evening for 24 weeks

Arm title	Trifarotene Vehicle Cream

Arm description:

Subjects applied Trifarotene vehicle cream on face once daily in the evening for 24 weeks.

Arm type	Active comparator
Investigational medicinal product name	Vehicle cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

Subjects applied Trifarotene Vehicle cream on face once daily in the evening for 24 weeks.

Number of subjects in period 1	Trifarotene Cream	Trifarotene Vehicle Cream
Started	60	63
Completed	45	53
Not completed	15	10
Non-Compliance with Investigational Product	1	1
Consent withdrawn by subject	3	1
Consent withdrawn by parent or guardian	2	1
Lost to follow-up	9	7

Baseline characteristics

Reporting groups	
Reporting group title	Trifarotene Cream
Reporting group description:	
Subjects applied Trifarotene 50 (mcg/g) cream on face once daily in the evening for 24 weeks.	
Reporting group title	Trifarotene Vehicle Cream
Reporting group description:	
Subjects applied Trifarotene vehicle cream on face once daily in the evening for 24 weeks.	

Reporting group values	Trifarotene Cream	Trifarotene Vehicle Cream	Total
Number of subjects	60	63	123
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)	15	18	33
Adults (18-64 years)	45	45	90
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	22.7	21.9	
standard deviation	± 6.30	± 5.95	-
Gender categorical Units: Subjects			
Female	45	48	93
Male	15	15	30
Ethnicity categorical Units: Subjects			
Hispanic or Latino	21	27	48
Not Hispanic or Latino	39	36	75
Unknown or Not Reported	0	0	0
Race categorical Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	11	6	17
Native Hawaiian or Other Pacific Islander	0	2	2
Black or African American	22	23	45
White	25	31	56
More than one race	0	0	0
Unknown or Not Reported	1	1	2

End points

End points reporting groups

Reporting group title	Trifarotene Cream
Reporting group description:	
Subjects applied Trifarotene 50 (mcg/g) cream on face once daily in the evening for 24 weeks.	
Reporting group title	Trifarotene Vehicle Cream
Reporting group description:	
Subjects applied Trifarotene vehicle cream on face once daily in the evening for 24 weeks.	

Primary: Absolute Change From Baseline in Post-Inflammatory Hyperpigmentation (PIH) Overall Disease Severity (ODS) Scores at Week 24

End point title	Absolute Change From Baseline in Post-Inflammatory Hyperpigmentation (PIH) Overall Disease Severity (ODS) Scores at Week 24
End point description:	
The PIH ODS Score is based on a 9-point scale: Grade 0 Normal; Grade 1- present, but less than (<) mild; Grade 2- mild (slightly noticeable); Grade 3- between mild and moderate; Grade 4- moderate; Grade 5- between moderate and marked; Grade 6- marked (distinctive); Grade 7- between marked and severe; Grade 8- severe (very distinctive) with higher grade indicating severe pigmentation. . A negative change indicates a reduction in PIH disease severity score from baseline. The intent-to-Treat (ITT) population included all subjects who were randomized.	
End point type	Primary
End point timeframe:	
Baseline, Week 24	

End point values	Trifarotene Cream	Trifarotene Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	63		
Units: score on a scale				
least squares mean (standard error)	-2.1 (± 0.27)	-2.1 (± 0.24)		

Statistical analyses

Statistical analysis title	Absolute Change in PIH ODS Scores at Week 24
Comparison groups	Trifarotene Cream v Trifarotene Vehicle Cream
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8879
Method	ANCOVA

Secondary: Percent Change From Baseline in PIH ODS Scores at Week 24

End point title	Percent Change From Baseline in PIH ODS Scores at Week 24

End point description:

The PIH ODS Score is based on a 9-point scale: Grade 0 Normal; Grade 1- present, but less than (<) mild; Grade 2- mild (slightly noticeable); Grade 3- between mild and moderate; Grade 4- moderate; Grade 5- between moderate and marked; Grade 6- marked (distinctive); Grade 7- between marked and severe; Grade 8- severe (very distinctive) with higher grade indicating severe pigmentation. . A negative change indicates a reduction in PIH disease severity score from baseline. The intent-to-Treat (ITT) population included all subjects who were randomized.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Trifarotene Cream	Trifarotene Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	63		
Units: percent change				
least squares mean (standard error)	-45.4 (± 5.73)	-44.9 (± 5.18)		

Statistical analyses

Statistical analysis title	% Change in PIH ODS Scores at Week 24
Comparison groups	Trifarotene Cream v Trifarotene Vehicle Cream
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9395
Method	ANCOVA

Secondary: Absolute Change From Baseline in PIH ODS Scores at Weeks 12, 16 and 20

End point title	Absolute Change From Baseline in PIH ODS Scores at Weeks 12, 16 and 20

End point description:

The PIH ODS Score is based on a 9-point scale: Grade 0 Normal; Grade 1- present, but less than (<) mild; Grade 2- mild (slightly noticeable); Grade 3- between mild and moderate; Grade 4- moderate; Grade 5- between moderate and marked; Grade 6- marked (distinctive); Grade 7- between marked and severe; Grade 8- severe (very distinctive) with higher grade indicating severe pigmentation. . A negative change indicates a reduction in PIH disease severity score from baseline. The intent-to-Treat (ITT) population included all subjects who were randomized.

End point type	Secondary

End point timeframe:

Baseline, Week 12, Week 16 and Week 20

End point values	Trifarotene Cream	Trifarotene Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	63		
Units: score on a scale				
least squares mean (standard error)				
Absolute Change at Week 12	-1.6 (± 0.18)	-1.1 (± 0.17)		
Absolute Change at Week 16	-1.9 (± 0.2)	-1.7 (± 0.19)		
Absolute Change at Week 20	-2.0 (± 0.22)	-1.9 (± 0.21)		

Statistical analyses

Statistical analysis title	Absolute Change in PIH ODS Scores at Week 12
Comparison groups	Trifarotene Cream v Trifarotene Vehicle Cream
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≥ 0.01
Method	ANCOVA

Statistical analysis title	Absolute Change in PIH ODS Scores at Week 16
Comparison groups	Trifarotene Cream v Trifarotene Vehicle Cream
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3332
Method	ANCOVA

Statistical analysis title	Absolute Change in PIH ODS Scores at Week 20
Comparison groups	Trifarotene Cream v Trifarotene Vehicle Cream
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6385
Method	ANCOVA

Secondary: Percent Change From Baseline in PIH ODS Scores at Weeks 12, 16 and 20

End point title	Percent Change From Baseline in PIH ODS Scores at Weeks 12, 16 and 20

End point description:

The PIH ODS Score is based on a 9-point scale: Grade 0 Normal; Grade 1- present, but less than (<) mild; Grade 2- mild (slightly noticeable); Grade 3- between mild and moderate; Grade 4- moderate; Grade 5- between moderate and marked; Grade 6- marked (distinctive); Grade 7- between marked and severe; Grade 8- severe (very distinctive) with higher grade indicating severe pigmentation. . A negative change indicates a reduction in PIH disease severity score from baseline. The intent-to-Treat (ITT) population included all subjects who were randomized.

End point type	Secondary

End point timeframe:

Baseline, Week 12, Week 16 and Week 20

End point values	Trifarotene Cream	Trifarotene Vehicle Cream		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	63		
Units: percent change				
least squares mean (standard error)				
Percent Change at Week 12	-34.4 (± 3.78)	-23.6 (± 3.60)		
Percent Change at Week 16	-41.2 (± 4.35)	-36.1 (± 4.17)		
Percent Change at Week 20	-43.9 (± 4.83)	-41.0 (± 4.75)		

Statistical analyses

Statistical analysis title	% Change in PIH ODS Scores at Week 12
Comparison groups	Trifarotene Cream v Trifarotene Vehicle Cream
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≥ 0.01
Method	ANCOVA

Statistical analysis title	% Change in PIH ODS Scores at Week 16
Comparison groups	Trifarotene Cream v Trifarotene Vehicle Cream
Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4039
Method	ANCOVA

Statistical analysis title	% Change in PIH ODS Scores at Week 20
Comparison groups	Trifarotene Cream v Trifarotene Vehicle Cream

Number of subjects included in analysis	123
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4039
Method	ANCOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From screening up to Week 24	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1
Reporting groups	
Reporting group title	Trifarotene Cream
Reporting group description: Subjects applied Trifarotene 50 (mcg/g) cream on face once daily in the evening for 24 weeks.	
Reporting group title	Trifarotene Vehicle Cream
Reporting group description: Subjects applied Trifarotene vehicle cream on face once daily in the evening for 24 weeks.	

Serious adverse events	Trifarotene Cream	Trifarotene Vehicle Cream	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Psychiatric disorders			
Bipolar Disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Trifarotene Cream	Trifarotene Vehicle Cream	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 60 (16.67%)	19 / 63 (30.16%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hair follicle tumour benign			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			

Ligament sprain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 60 (0.00%)	2 / 63 (3.17%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Application site burn			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	1 / 60 (1.67%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 60 (0.00%)	2 / 63 (3.17%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 60 (1.67%)	1 / 63 (1.59%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Psychiatric disorders			

Attention deficit hyperactivity disorder			
subjects affected / exposed	1 / 60 (1.67%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Bipolar I disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	1 / 60 (1.67%)	0 / 63 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Bacterial vaginosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	3 / 60 (5.00%)	6 / 63 (9.52%)	
occurrences (all)	3	6	
Ear infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	2 / 60 (3.33%)	1 / 63 (1.59%)	
occurrences (all)	2	1	
Nasopharyngitis			
subjects affected / exposed	2 / 60 (3.33%)	1 / 63 (1.59%)	
occurrences (all)	2	1	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 63 (1.59%)	
occurrences (all)	0	1	
Vaginal infection			

subjects affected / exposed occurrences (all)	0 / 60 (0.00%) 0	1 / 63 (1.59%) 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