Clinical trial results:
Evaluation of the Risk of Atrophic Acne Scar Formation During Treatment of Acne Vulgaris Subjects With Trifarotene 50 mcg/g Cream Versus Vehicle Cream Over 24 Weeks

Summary

EudraCT number	2020-006050-51
Trial protocol	FR
Global end of trial date	09 February 2023

Results information

Result version number	v1 (current)
This version publication date	05 April 2024
First version publication date	05 April 2024

Trial information

Trial identification

Sponsor protocol code	RD.06.SPR.202395

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04856904
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galderma S.A.
Sponsor organisation address	Zahlerweg 10, 6300 Zug, ZUG, Switzerland, 6300
Public contact	Clinical Trial Information Desk, CTD Coordinator Galderma R&D S.A., ctacoordinator@galderma.com
Scientific contact	Clinical Trial Information Desk, CTD Coordinator Galderma R&D S.A., ctacoordinator@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	03 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 February 2023
Global end of trial reached?	Yes
Global end of trial date	09 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this clinical study was to evaluate the effect of trifarotene compared to its vehicle on the risk of formation of atrophic acne scars after 24 weeks of treatment in facial acne subjects assessed by atrophic acne scars count.

Protection of trial subjects:

This clinical study was conducted in accordance with the protocol, the Declaration of Helsinki, and the International Conference on Harmonization Good Clinical Practices (ICH GCP), and in compliance with other applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 May 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	France: 2
Country: Number of subjects enrolled	United States: 110
Country: Number of subjects enrolled	Canada: 9
Worldwide total number of subjects	121
EEA total number of subjects	2

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)	19
Adults (18-64 years)	102
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 20 sites in the United States, Canada, and France from 26 May 2021 to 9 February 2023.

Pre-assignment

Screening details:

A total 121 subjects were enrolled in this study. All subjects were randomized (left face versus right face) to apply trifarotene cream and trifarotene vehicle cream for an intra-individual, split-face comparison.

Period 1

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

Arms

Arm title	All Acne Vulgaris Subjects

Arm description:

All subjects applied a thin layer of trifarotene 50 microgram per gram (mcg/g) cream to half of their face and trifarotene vehicle cream to another half of their face topically once daily for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Trifarotene 50mcg/g cream
Investigational medicinal product code	CD5789
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Subjects applied a thin layer of trifarotene cream to half of their face topically once daily.

Investigational medicinal product name	Trifarotene Vehicle Cream
Investigational medicinal product code	
Other name	Placebo
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Subjects applied a thin layer of trifarotene vehicle cream to another half of their face topically once daily.

Number of subjects in period 1	All Acne Vulgaris Subjects
Started	121
Trifarotene 50mcg/g cream	121
Trifarotene Vehicle	121
Completed	99
Not completed	22
Physician decision	1

Adverse event, non-fatal	1
Non-compliance with study drug	1
Lost to follow-up	4
Withdrawal by parent/guardian	1
Protocol deviation	1
Withdrawal by subject	13

Baseline characteristics

Reporting groups	
Reporting group title	All Acne Vulgaris Subjects
Reporting group description:	
All subjects applied a thin layer of trifarotene 50 microgram per gram (mcg/g) cream to half of their face and trifarotene vehicle cream to another half of their face topically once daily for up to 24 weeks.	

Reporting group values	All Acne Vulgaris Subjects	Total	
Number of subjects	121	121	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	22.9		
standard deviation	± 5.12	-	
Gender categorical			
Units: Subjects			
Female	88	88	
Male	33	33	
Ethinicity			
Units: Subjects			
Hispanic or Latino	26	26	
Not Hispanic or Latino	95	95	
Race			
Units: Subjects			
White	97	97	
Black or African American	9	9	
Asian	12	12	
Not Reported	3	3	
Fitzpatrick Skin Type			
Skin Type I = White; very fair, red or blonde hair blue eyes; freckles; Always burns, never tans Skin Type II = White, fair, red or blond hair; blue, hazel or green eyes; Usually burns, tans with difficulty Skin Type III = Cream white; fair with any eye or hair color (common); Sometimes mild burn, gradually tans Skin Type IV = Brown; typical Mediterranean Caucasian skin; Rarely burns, tans with ease Skin Type V = Dark Brown; mid-eastern skin types; Very rarely burns, tans easily Skin Type VI = Black; Never burns, tans very easily			
Units: Subjects			
Type I	7	7	
Type II	43	43	
Type III	31	31	
Type IV	26	26	
Type V	11	11	
Type VI	3	3	

End points

End points reporting groups

Reporting group title	All Acne Vulgaris Subjects

Reporting group description:

All subjects applied a thin layer of trifarotene 50 microgram per gram (mcg/g) cream to half of their face and trifarotene vehicle cream to another half of their face topically once daily for up to 24 weeks.

Subject analysis set title	Trifarotene 50 mcg/g Cream
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects applied a thin layer of trifarotene 50 mcg/g cream to half of their face and topically once daily for up to 24 weeks.

Subject analysis set title	Trifarotene vehicle cream
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects applied a thin layer of trifarotene vehicle cream to another half of their face topically once daily for up to 24 weeks.

Primary: Absolute Change From Baseline in Total Atrophic Acne Scar Count Per Half Face at Week 24

End point title	Absolute Change From Baseline in Total Atrophic Acne Scar Count Per Half Face at Week 24

End point description:

The scars were counted according to their size defined in two categories using 2 millimeter (mm) and 4 mm punch biopsy tools for size classification: 1) atrophic scars 2 to 4 mm: included boxcar (sheer edges), rolling (irregular surface), and undetermined types; 2) atrophic scars greater than (>) 4 mm: included boxcar (sheer edges), rolling (irregular surface), and undetermined types. Each type of atrophic acne scar was counted separately for each half-face by the evaluator for following regions: right forehead, right cheek, right side of the chin, left forehead, left cheek and left side of the chin. To obtain the total number of atrophic scars per half-face, atrophic acne scar counts for each half-face was added. ITT population included all randomized subjects.

End point type	Primary

End point timeframe:

Baseline, Week 24

End point values	Trifarotene 50 mcg/g Cream	Trifarotene vehicle cream		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	121	121		
Units: atrophic acne scars				
arithmetic mean (standard error)	-5.9 (± 0.51)	-2.7 (± 0.37)		

Statistical analyses

Statistical analysis title	Trifarotene 50 mcg/g, vehicle cream

Statistical analysis description:

Numbers reflecting in field "Number of subjects included in analysis" below is incorrect and this is due to constraints of the database. Consider the total number of subjects included in the analysis as 121. Each half of the face was analysed separately, thus 242 facial halves were analysed.

Comparison groups	Trifarotene 50 mcg/g Cream v Trifarotene vehicle cream
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Student's t-test for paired samples
Parameter estimate	Bilateral difference
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	-2
Variability estimate	Standard error of the mean
Dispersion value	0.6

Secondary: Absolute Change from Baseline in Total Atrophic Acne Scar Count Per Half Face up to Week 20

End point title	Absolute Change from Baseline in Total Atrophic Acne Scar Count Per Half Face up to Week 20

End point description:

The scars were counted according to their size defined in two categories using 2 mm and 4 mm punch biopsy tools for size classification: 1) atrophic scars 2 to 4 mm: included boxcar (sheer edges), rolling (irregular surface), and undetermined types; 2) atrophic scars > 4 mm: included boxcar (sheer edges), rolling (irregular surface), and undetermined types. Each type of atrophic acne scar was counted separately for each half-face by the evaluator for following regions: right forehead, right cheek, right side of the chin, left forehead, left cheek and left side of the chin. To obtain the total number of atrophic scars per half-face, atrophic acne scar counts for each half-face was added. ITT population included all randomized subjects.

End point type	Secondary

End point timeframe:

Baseline up to Week 20

End point values	Trifarotene 50 mcg/g Cream	Trifarotene vehicle cream		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	121	121		
Units: atrophic acne scars				
arithmetic mean (standard error)				
Week 1	-0.3 (± 0.21)	-0.3 (± 0.16)		
Week 2	-0.9 (± 0.26)	-0.4 (± 0.11)		
Week 4	-1.5 (± 0.27)	-0.7 (± 0.18)		
Week 8	-2.5 (± 0.30)	-1.1 (± 0.30)		
Week 12	-3.8 (± 0.37)	-1.7 (± 0.32)		
Week 16	-4.4 (± 0.40)	-1.7 (± 0.47)		
Week 20	-5.0 (± 0.47)	-2.5 (± 0.33)		

Statistical analyses

Statistical analysis title	Week 1: Trifarotene 50 mcg/g, vehicle cream

Statistical analysis description:

Numbers reflecting in field "Number of subjects included in analysis" below is incorrect and this is due to constraints of the database. Consider the total number of subjects included in the analysis as 121. Each half of the face was analysed separately, thus 242 facial halves were analysed.

Comparison groups	Trifarotene 50 mcg/g Cream v Trifarotene vehicle cream
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9476
Method	Student's t-test for paired samples
Parameter estimate	Bilateral difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.14

Statistical analysis title	Week 2: Trifarotene 50 mcg/g, vehicle cream

Statistical analysis description:

Numbers reflecting in field "Number of subjects included in analysis" below is incorrect and this is due to constraints of the database. Consider the total number of subjects included in the analysis as 121. Each half of the face was analysed separately, thus 242 facial halves were analysed.

Comparison groups	Trifarotene 50 mcg/g Cream v Trifarotene vehicle cream
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0248
Method	Student's t-test for paired samples
Parameter estimate	Bilateral difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.25

Statistical analysis title	Week 4: Trifarotene 50 mcg/g, vehicle cream
Statistical analysis description:	
Numbers reflecting in field "Number of subjects included in analysis" below is incorrect and this is due to constraints of the database. Consider the total number of subjects included in the analysis as 121. Each half of the face was analysed separately, thus 242 facial halves were analysed.	
Comparison groups	Trifarotene 50 mcg/g Cream v Trifarotene vehicle cream
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0072
Method	Student's t-test for paired samples
Parameter estimate	Bilateral difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.2
Variability estimate	Standard error of the mean
Dispersion value	0.29

Statistical analysis title	Week 8: Trifarotene 50 mcg/g, vehicle cream
Statistical analysis description:	
Numbers reflecting in field "Number of subjects included in analysis" below is incorrect and this is due to constraints of the database. Consider the total number of subjects included in the analysis as 121. Each half of the face was analysed separately, thus 242 facial halves were analysed.	
Comparison groups	Trifarotene 50 mcg/g Cream v Trifarotene vehicle cream
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Student's t-test for paired samples
Parameter estimate	Bilateral difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.35

Statistical analysis title	Week 12: Trifarotene 50 mcg/g, vehicle cream

Statistical analysis description:

Numbers reflecting in field "Number of subjects included in analysis" below is incorrect and this is due to constraints of the database. Consider the total number of subjects included in the analysis as 121. Each half of the face was analysed separately, thus 242 facial halves were analysed.

Comparison groups	Trifarotene 50 mcg/g Cream v Trifarotene vehicle cream
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Student's t-test for paired samples
Parameter estimate	Bilateral difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.41

Statistical analysis title	Week 16: Trifarotene 50 mcg/g, vehicle cream

Statistical analysis description:

Numbers reflecting in field "Number of subjects included in analysis" below is incorrect and this is due to constraints of the database. Consider the total number of subjects included in the analysis as 121. Each half of the face was analysed separately, thus 242 facial halves were analysed.

Comparison groups	Trifarotene 50 mcg/g Cream v Trifarotene vehicle cream
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Student's t-test for paired samples
Parameter estimate	Bilateral difference
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	-1.6
Variability estimate	Standard error of the mean
Dispersion value	0.56

Statistical analysis title	Week 20: Trifarotene 50 mcg/g, vehicle cream

Statistical analysis description:

Numbers reflecting in field "Number of subjects included in analysis" below is incorrect and this is due to constraints of the database. Consider the total number of subjects included in the analysis as 121. Each half of the face was analysed separately, thus 242 facial halves were analysed.

Comparison groups	Trifarotene 50 mcg/g Cream v Trifarotene vehicle cream

Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Student's t-test for paired samples
Parameter estimate	Bilateral difference
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	-1.5
Variability estimate	Standard error of the mean
Dispersion value	0.53

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From screening up to Week 28	
Adverse event reporting additional description:	
The safety (SAF) population included the ITT population subjects who applied the study drug at least once.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

Reporting groups	
Reporting group title	All Acne Vulgaris Subjects
Reporting group description:	
All subjects applied a thin layer of trifarotene 50 microgram per gram (mcg/g) cream to half of their face and trifarotene vehicle cream to another half of their face topically once daily for up to 24 weeks.	

Serious adverse events	All Acne Vulgaris Subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 121 (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 %

Non-serious adverse events	All Acne Vulgaris Subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 121 (27.27%)		
Investigations			
SARS-CoV-2 test positive			
subjects affected / exposed	2 / 121 (1.65%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	1 / 121 (0.83%)		
occurrences (all)	1		
Arthropod bite			

subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Hand fracture subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Skin laceration subjects affected / exposed occurrences (all)	2 / 121 (1.65%) 2		
Nervous system disorders			
Burning sensation subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Headache subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Pre syncope subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Somnolence subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
General disorders and administration site conditions			
Adverse reaction subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Face oedema subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Influenza like illness subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 2		
Vaccination site pain subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Immune system disorders			

Food allergy subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Food poisoning subjects affected / exposed occurrences (all) Haemorrhoids subjects affected / exposed occurrences (all) Hyperaesthesia teeth subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 1 / 121 (0.83%) 1 1 / 121 (0.83%) 1 1 / 121 (0.83%) 1 1 / 121 (0.83%) 1 1 / 121 (0.83%) 1 1 / 121 (0.83%) 1 1 / 121 (0.83%) 1		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all) Sinus congestion subjects affected / exposed occurrences (all)	 1 / 121 (0.83%) 1 1 / 121 (0.83%) 1		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	 1 / 121 (0.83%) 1		

Dermatitis contact subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Skin irritation subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Pruritus subjects affected / exposed occurrences (all)	2 / 121 (1.65%) 2		
Rash subjects affected / exposed occurrences (all)	2 / 121 (1.65%) 2		
Skin tightness subjects affected / exposed occurrences (all)	2 / 121 (1.65%) 3		
Psychiatric disorders Agitation subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Anxiety subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Musculoskeletal and connective tissue disorders Neck pain subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Infections and infestations Gastroenteritis viral subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Kidney infection subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Tooth abscess subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		

Urinary tract infection subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
Viral infection subjects affected / exposed occurrences (all)	1 / 121 (0.83%) 1		
COVID-19 subjects affected / exposed occurrences (all)	10 / 121 (8.26%) 10		
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 121 (1.65%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 May 2021	Amendment 1: The protocol was revised to address the following typographical errors for document consistency and clarity.
09 July 2021	Amendment 2: -SCARS questionnaire sample facial image (all pages) and reference to proper side of face . -Subject Satisfaction questionnaire sample facial image. -Inclusion criteria minimum atrophic acne scar size (>=2mm) -Authorized medications and clarity of final study visit (Week 24). Prohibited Medications/Therapies a. include testosterone supplements for consistency with Exclusion Criterion 12 b. omit restrictions that are not applicable (use of antacids, iron-containing supplements) -Summaries of bilateral difference between treatments can be presented only overall and not by treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported