



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) | EMA-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 (\pm 0.27) | -2.1 (\pm 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 (\pm 0.18) | -1.1 (\pm 0.17) | | |
| Absolute Change at Week 16 | -1.9 (\pm 0.2) | -1.7 (\pm 0.19) | | |
| Absolute Change at Week 20 | -2.0 (\pm 0.22) | -1.9 (\pm 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 occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 63 (1.59%) 1 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 2 / 63 (3.17%) 2 | |
| General disorders and administration site conditions Application site burn subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 63 (1.59%) 1 | |
| Eye disorders Eye irritation subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 63 (1.59%) 1 | |
| Gastrointestinal disorders Toothache subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 1 / 60 (1.67%) 1 | 1 / 63 (1.59%) 1 0 / 63 (0.00%) 0 | |
| Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 2 / 63 (3.17%) 2 | |
| Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | 1 / 63 (1.59%) 1 | |
| Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 63 (1.59%) 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 | 0 / 60 (0.00%) | 1 / 63 (1.59%) | |
| occurrences (all) | 0 | 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