

**Clinical trial results:****A Multi-Center, Randomized, Double-Blind, Parallel-Group Vehicle Controlled Study To Compare The Efficacy And Safety Of CD5789 50g/g Cream Versus Vehicle Cream In Subjects With Acne Vulgaris
Summary**

| | |
|--------------------------|----------------|
| EudraCT number | 2015-002540-13 |
| Trial protocol | HU ES CZ |
| Global end of trial date | 12 May 2017 |

Results information

| | |
|-----------------------------------|--------------------------------|
| Result version number | v1 (current) |
| This version publication date | 11 January 2020 |
| First version publication date | 11 January 2020 |
| Summary attachment (see zip file) | Synopsis (RD.06.SRE.18252.pdf) |

Trial information**Trial identification**

| | |
|-----------------------|-----------------|
| Sponsor protocol code | RD.06.SPR.18252 |
|-----------------------|-----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02556788 |
| 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 | CTA Coordinator, Galderma S.A., +41 21 642 78 00, cta.coordinator@galderma.com |
| Scientific contact | CTA Coordinator, Galderma S.A., +41 21 642 78 00, cta.coordinator@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? | Yes |
| 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 | 31 October 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 07 February 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 May 2017 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Multi-center, randomized, double blind, vehicle controlled study, to assess the efficacy and safety of CD5789 50 microgram/g cream in subjects 9 years of age and older with moderate acne vulgaris on face and trunk, when applied once daily for 12 weeks.

Protection of trial subjects:

All subjects were required to read and sign an informed consent. The subjects could withdraw from the treatment at any time and for any reason.

Background therapy:

Not Applicable

Evidence for comparator:

Not Applicable

| | |
|---|------------------|
| Actual start date of recruitment | 23 November 2015 |
| 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 | Poland: 188 |
| Country: Number of subjects enrolled | Romania: 129 |
| Country: Number of subjects enrolled | Spain: 28 |
| Country: Number of subjects enrolled | Czech Republic: 123 |
| Country: Number of subjects enrolled | Hungary: 140 |
| Country: Number of subjects enrolled | Russian Federation: 181 |
| Country: Number of subjects enrolled | Ukraine: 145 |
| Country: Number of subjects enrolled | United States: 278 |
| Worldwide total number of subjects | 1212 |
| EEA total number of subjects | 608 |

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) | 15 |
| Adolescents (12-17 years) | 555 |
| Adults (18-64 years) | 642 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 1212 subjects were enrolled and exposed to CD5789 50 microgram/g cream or vehicle cream for 12 weeks. A minimum of 14 days between Screening and Baseline visit (+/- 3 days). Study visits for Weeks 1,2,4,8 (+/- 3 days) and Week 12 (+/- 5 days).

Pre-assignment

Screening details:

Male or Female subjects, 9 years of age and older, with moderate acne vulgaris, with at least 20 inflammatory lesions and 25 non-inflammatory lesions for face, and , at least 20 inflammatory and 20-100 non-inflammatory on the trunk. No more than 1 nodule on the face and trunk. Inclusion criteria for trunk was optional for subjects ages 9 to 11.

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 | Subject, Investigator |

Arms

| | |
|--|-----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | CD5789 50 microgram/g cream |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | CD5789 50 microgram/g cream |
| Investigational medicinal product code | CD5789 |
| Other name | trifarotene |
| Pharmaceutical forms | Cream |
| Routes of administration | Cutaneous use |

Dosage and administration details:

A thin layer of study product cream (one pump actuation) was applied to the face region: forehead, nose, chin, area between the nose and upper lip, and each cheek. Avoid application proximity in/close to eyes, angles of mouth, lips and mucous membranes.

A thin layer of study product cream (two pump actuations) was applied to the truncal region: right and left upper back, right and left shoulders and right and left anterior chest, self-reachable by the subject. Avoid application to axillary region, anterior and posterior neck.

Apply daily, in the evening, for 12 weeks, after washing the treated areas with preferred mild or soapless cleanser and allow to fully dry before applying study drug. The use of non comedogenic moisturizer was encouraged to be used as desired but respecting an interval of 1 hour (before and after) study drug application.

| | |
|--|---------------|
| Arm title | Vehicle cream |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Vehicle cream |
| Investigational medicinal product code | N/A |
| Other name | placebo |
| Pharmaceutical forms | Cream |
| Routes of administration | Cutaneous use |

Dosage and administration details:

A thin layer of study product cream (one pump actuation) was applied to the face region: forehead, nose, chin, area between the nose and upper lip, and each cheek. Avoid application proximity in/close to eyes, angles of mouth, lips and mucous membranes.

A thin layer of study product cream (two pump actuations) was applied to the truncal region: right and left upper back, right and left shoulders and right and left anterior chest, self-reachable by the subject. Avoid application to axillary region, anterior and posterior neck.

Apply daily, in the evening, for 12 weeks, after washing the treated areas with preferred mild or soapless cleanser and allow to fully dry before applying study drug. The use of non comedogenic moisturizer was encouraged to be used as desired but respecting an interval of 1 hour (before and after) study drug application.

| Number of subjects in period 1 | CD5789 50 microgram/g cream | Vehicle cream |
|---------------------------------------|--------------------------------|---------------|
| Started | 602 | 610 |
| Completed | 558 | 573 |
| Not completed | 44 | 37 |
| Consent withdrawn by subject | 18 | 21 |
| Adverse event, non-fatal | 9 | 1 |
| Protocol violation | 4 | 1 |
| Other | - | 1 |
| Pregnancy | 1 | 1 |
| Other reasons | 3 | - |
| Lost to follow-up | 9 | 11 |
| Lack of efficacy | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | CD5789 50 microgram/g cream |
|-----------------------|-----------------------------|

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| | |
|-----------------------|---------------|
| Reporting group title | Vehicle cream |
|-----------------------|---------------|

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| Reporting group values | CD5789 50 microgram/g cream | Vehicle cream | Total |
|--|-----------------------------|---------------|-------|
| Number of subjects | 602 | 610 | 1212 |
| 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) | 9 | 6 | 15 |
| Adolescents (12-17 years) | 267 | 288 | 555 |
| Adults (18-64 years) | 326 | 316 | 642 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous Units: years | | | |
| arithmetic mean | 19.6 | 19.9 | |
| standard deviation | ± 6.20 | ± 6.38 | - |
| Gender categorical Units: Subjects | | | |
| Female | 357 | 338 | 695 |
| Male | 245 | 272 | 517 |

End points

End points reporting groups

| | |
|--------------------------------|-----------------------------|
| Reporting group title | CD5789 50 microgram/g cream |
| Reporting group description: - | |
| Reporting group title | Vehicle cream |
| Reporting group description: - | |

Primary: Absolute Change in Inflammatory Lesion Count (Face)

| | |
|------------------------|---|
| End point title | Absolute Change in Inflammatory Lesion Count (Face) |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| Baseline to Week 12 | |

| End point values | CD5789 50 microgram/g cream | Vehicle cream | | |
|-------------------------------------|-----------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 602 | 610 | | |
| Units: Absolute Change in Lesions | | | | |
| least squares mean (standard error) | -24.2 (± 0.51) | -18.7 (± 0.51) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Change in Facial Inflammatory Lesion Counts |
| Comparison groups | CD5789 50 microgram/g cream v Vehicle cream |
| Number of subjects included in analysis | 1212 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -5.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.9 |
| upper limit | -4.3 |
| Variability estimate | Standard deviation |

Primary: Absolute Change in Non Inflammatory Lesions (Face)

| | |
|-----------------|--|
| End point title | Absolute Change in Non Inflammatory Lesions (Face) |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline to Week 12

| End point values | CD5789 50 microgram/g cream | Vehicle cream | | |
|-------------------------------------|-----------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 602 | 610 | | |
| Units: Absolute Change in Lesions | | | | |
| least squares mean (standard error) | -30.1 (± 0.71) | -21.6 (± 0.71) | | |

Statistical analyses

| Statistical analysis title | Absolute Change in Non-Inflammatory (Face) |
|---|---|
| Comparison groups | CD5789 50 microgram/g cream v Vehicle cream |
| Number of subjects included in analysis | 1212 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | ANCOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -8.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.3 |
| upper limit | -6.6 |
| Variability estimate | Standard deviation |

Primary: IGA Success Rate

| | |
|-----------------|------------------|
| End point title | IGA Success Rate |
|-----------------|------------------|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline to Week 12

| | | | | |
|-----------------------------|-----------------------------|-----------------|--|--|
| End point values | CD5789 50 microgram/g cream | Vehicle cream | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 602 | 610 | | |
| Units: Percentage | | | | |
| number (not applicable) | 42.3 | 25.7 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | IGA Success Rate |
| Comparison groups | CD5789 50 microgram/g cream v Vehicle cream |
| Number of subjects included in analysis | 1212 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 16.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 11.3 |
| upper limit | 22 |
| Variability estimate | Standard deviation |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to Week 12

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Vehicle |
|-----------------------|---------|

Reporting group description: -

| | |
|-----------------------|--------------------------|
| Reporting group title | CD5789 50 microgram/gram |
|-----------------------|--------------------------|

Reporting group description: -

| Serious adverse events | Vehicle | CD5789 50 microgram/gram | |
|---|-----------------|--------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 609 (0.66%) | 2 / 602 (0.33%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Ligament Sprain | | | |
| subjects affected / exposed ^[1] | 1 / 1 (100.00%) | 1 / 1 (100.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed ^[2] | 1 / 1 (100.00%) | 0 / 1 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Suicide Attempt | | | |
| subjects affected / exposed ^[3] | 1 / 1 (100.00%) | 1 / 1 (100.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Major Depression | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed ^[4] | 0 / 1 (0.00%) | 1 / 1 (100.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Sinusitis | | | |
| subjects affected / exposed ^[5] | 1 / 1 (100.00%) | 0 / 1 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed ^[6] | 1 / 1 (100.00%) | 0 / 1 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This is correct as reported.

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | Vehicle | CD5789 50 microgram/gram | |
|---|------------------|--------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 21 / 609 (3.45%) | 45 / 602 (7.48%) | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed ^[7] | 1 / 1 (100.00%) | 0 / 1 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood creatine increased | | | |
| subjects affected / exposed ^[8] | 1 / 1 (100.00%) | 0 / 1 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|--|-----------------|-------------------|--|
| Injury, poisoning and procedural complications | | | |
| Sunburn | | | |
| subjects affected / exposed ^[9] | 0 / 1 (0.00%) | 2 / 2 (100.00%) | |
| occurrences (all) | 0 | 2 | |
| Drug administered at inappropriate site | | | |
| subjects affected / exposed ^[10] | 0 / 1 (0.00%) | 1 / 1 (100.00%) | |
| occurrences (all) | 0 | 1 | |
| Blood and lymphatic system disorders | | | |
| Lymphadenopathy | | | |
| subjects affected / exposed ^[11] | 0 / 1 (0.00%) | 1 / 1 (100.00%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Application site irritation | | | |
| subjects affected / exposed ^[12] | 0 / 1 (0.00%) | 15 / 15 (100.00%) | |
| occurrences (all) | 0 | 15 | |
| Application site pruritus | | | |
| subjects affected / exposed ^[13] | 2 / 2 (100.00%) | 5 / 5 (100.00%) | |
| occurrences (all) | 2 | 5 | |
| Application site pain | | | |
| subjects affected / exposed ^[14] | 0 / 1 (0.00%) | 4 / 4 (100.00%) | |
| occurrences (all) | 0 | 4 | |
| Application site dryness | | | |
| subjects affected / exposed ^[15] | 0 / 1 (0.00%) | 3 / 3 (100.00%) | |
| occurrences (all) | 0 | 3 | |
| Application site erosion | | | |
| subjects affected / exposed ^[16] | 0 / 1 (0.00%) | 1 / 1 (100.00%) | |
| occurrences (all) | 0 | 1 | |
| Application site erythema | | | |
| subjects affected / exposed ^[17] | 0 / 1 (0.00%) | 1 / 1 (100.00%) | |
| occurrences (all) | 0 | 1 | |
| Eye disorders | | | |
| Eyelid exfoliation | | | |
| subjects affected / exposed ^[18] | 0 / 1 (0.00%) | 1 / 1 (100.00%) | |
| occurrences (all) | 0 | 1 | |
| Eyelid oedema | | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed ^[19] occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 1 (100.00%) 1 | |
| Gastrointestinal disorders Cheilitis subjects affected / exposed ^[20] occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 1 (100.00%) 1 | |
| Skin and subcutaneous tissue disorders Skin irritation subjects affected / exposed ^[21] occurrences (all) Skin fissures subjects affected / exposed ^[22] occurrences (all) | 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 | 2 / 2 (100.00%) 2 1 / 1 (100.00%) 1 | |
| Psychiatric disorders Insomnia subjects affected / exposed ^[23] occurrences (all) | 0 / 1 (0.00%) 0 | 1 / 1 (100.00%) 1 | |
| Infections and infestations Herpes simplex subjects affected / exposed ^[24] occurrences (all) Tinea versicolour subjects affected / exposed ^[25] occurrences (all) Oral herpes subjects affected / exposed ^[26] occurrences (all) | 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 1 / 1 (100.00%) 1 | 1 / 1 (100.00%) 1 1 / 1 (100.00%) 1 0 / 1 (0.00%) 0 | |

Notes:

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This is correct as reported.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This is correct as reported.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This is correct as reported.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This is correct as reported.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects

Justification: This is correct as reported.

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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 19 January 2017 | Major changes included in the Protocol: 1. Increase in the number of investigational centers from 75 to 85 centers 2. Russian Minister of Health request to edit wording of inclusion criteria number 1 to better reflect the age groups. 3. Japan was removed from the region(s)/countries involved in the study |
| 24 February 2017 | Major changes included in the PIP: Due to the unexpected slow recruitment for subjects aged less 14 years old and 14 to 17 years old: a. Extension of study completion from October 2016 to August 2017; b. Modification of the agreed paediatric investigation plan to decrease the number of paediatric subjects enrollment. Request was accepted by the Pediatric Committee. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Not Applicable

Notes: