



## Clinical trial results:

### Effect of CD07805/47 gel in subjects presenting with flushing related to erythematotelangiectatic or papulopustular rosacea

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2013-005083-26 |
| Trial protocol           | DE             |
| Global end of trial date | 30 June 2014   |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 20 February 2016 |
| First version publication date | 20 February 2016 |

#### Trial information

##### Trial identification

|                       |                  |
|-----------------------|------------------|
| Sponsor protocol code | RD.03.SPR.40225E |
|-----------------------|------------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02300129 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Galderma R&D SNC   |
| Sponsor organisation address | Les Templiers, 2400 Route des Colles , Biot, France, 06410                           |
| Public contact               | CTA Coordinator, Galderma R&D SNC, +33 (0)493-95-70-85, cta.coordinator@galderma.com |
| Scientific contact           | CTA Coordinator, Galderma R&D SNC, +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:

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**Results analysis stage**

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|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 12 February 2015 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 30 June 2014     |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 30 June 2014     |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

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Main objective of the trial:

- to demonstrate objectively that CD07805/47 0.5% gel is able to prevent a flush induced by a specific trigger (hot water) in controlled condition;
- to demonstrate that CD07805/47 0.5% gel is able to prevent a flush whatever the trigger in everyday life condition;
- to investigate if reduction in redness is associated with a decrease in skin sensations such as heat, burning/stinging, skin tension and sweating;
- to demonstrate that such efficacy on transient redness and sensations takes place in both populations (rosacea type I and rosacea type II).

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 14 April 2014 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 34 |
| Worldwide total number of subjects   | 34          |
| EEA total number of subjects         | 34          |

Notes:

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**Subjects enrolled per age group**

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|   |   |
|---|---|
| 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)      | 32 |
| From 65 to 84 years       | 2  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at 1 investigative site in Germany from 14 April 2014 to 30 June 2014

### Pre-assignment

Screening details:

A total of 46 subjects were screened, 34 were randomised for Period 1, and 32 participated in Period 2.

### Period 1

|                              |                         |
|------------------------------|-------------------------|
| Period 1 title               | Flush model             |
| Is this the baseline period? | Yes                     |
| Allocation method            | Randomised - controlled |
| Blinding used                | Double blind            |
| Roles blinded                | Investigator, Subject   |

### Arms

|           |             |
|-----------|-------------|
| Arm title | flush model |
|-----------|-------------|

Arm description:

The period 1 (1 week) includes cross-over (first and third sessions) and split face design (second session). During this period, the study drugs are applied as follows:

placebo gel on both sides on face;

one side of the face treated with CD07805/47 0.5% gel and the other side with CD07805/47 placebo gel (allocation of treatment on each half-face is randomized)

CD07805/47 0.5% gel on both sides on face

|  |                      |
|--|----------------------|
| Arm type                               | Experimental         |
| Investigational medicinal product name | Brimonidine tartrate |
| Investigational medicinal product code | CD07805/47           |
| Other name                             |                      |
| Pharmaceutical forms                   | Gel                  |
| Routes of administration               | Cutaneous use        |

Dosage and administration details:

CD07805/47 0.5% gel

|  |                        |
|--|------------------------|
| Investigational medicinal product name | CD07805/47 placebo Gel |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Gel                    |
| Routes of administration               | Cutaneous use          |

Dosage and administration details:

placebo gel

| <b>Number of subjects in period 1[1]</b> | flush model |
|--|-------------|
| Started                                  | 33          |
| Completed                                | 32          |
| Not completed                            | 1           |
| Consent withdrawn by subject             | 1           |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One subject was excluded from ITT (intent to treat) population because he didn't perform any efficacy assessment during the study so N=33 instead of 34 subjects

## Period 2

|                              |                         |
|------------------------------|-------------------------|
| Period 2 title               | Cross over              |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Double blind            |
| Roles blinded                | Subject, Investigator   |

## Arms

|                              |                                |
|------------------------------|--------------------------------|
| Are arms mutually exclusive? | No                             |
| <b>Arm title</b>             | CD07805/47 0.5% gel cross over |

Arm description:

The period 2 (4 weeks) corresponds to a cross-over design. The CD07805/47 0.5% gel is applied once a day on the whole face and then the CD07805/47 placebo gel for the 2 following weeks or inversely according to randomisation

|  |                      |
|--|----------------------|
| Arm type                               | Experimental         |
| Investigational medicinal product name | Brimonidine tartrate |
| Investigational medicinal product code | CD07805/47           |
| Other name                             |                      |
| Pharmaceutical forms                   | Gel                  |
| Routes of administration               | Cutaneous use        |

Dosage and administration details:

CD07805 0.5% gel once a day during 2 weeks

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | CD07805/47 Placebo gel cross-over |
|------------------|-----------------------------------|

Arm description:

The period 2 (4 weeks) corresponds to a cross-over design. The CD07805/47 0.5% gel is applied once a day on the whole face and then the CD07805/47 placebo gel for the 2 following weeks or inversely according to randomization

|  |                        |
|--|------------------------|
| Arm type                               | Placebo                |
| Investigational medicinal product name | CD07805/47 Placebo gel |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Gel                    |
| Routes of administration               | Cutaneous use          |

Dosage and administration details:

placebo once a day during 2 weeks

| <b>Number of subjects in period 2</b> | CD07805/47 0.5%<br>gel cross over | CD07805/47 Placebo<br>gel cross-over |
|---------------------------------------|-----------------------------------|--------------------------------------|
| Started                               | 32                                | 32                                   |
| Completed                             | 31                                | 31                                   |
| Not completed                         | 1                                 | 1                                    |
| Adverse event, non-fatal              | 1                                 | 1                                    |

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Flush model |
|-----------------------|-------------|

Reporting group description: -

| Reporting group values                             | Flush model | Total |  |
|--|-------------|-------|--|
| Number of subjects                                 | 33          | 33    |  |
| Age categorical                                    |             |       |  |
| All subjects included in Period 1 (flush model)    |             |       |  |
| Units: Subjects                                    |             |       |  |
| In utero   | 0           | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0           | 0     |  |
| Newborns (0-27 days)                               | 0           | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0           | 0     |  |
| Children (2-11 years)                              | 0           | 0     |  |
| Adolescents (12-17 years)                          | 0           | 0     |  |
| Adults (18-64 years)                               | 31          | 31    |  |
| From 65-84 years                                   | 2           | 2     |  |
| 85 years and over                                  | 0           | 0     |  |
| Age continuous                                     |             |       |  |
| Units: years                                       |             |       |  |
| arithmetic mean                                    | 50.2        |       |  |
| standard deviation                                 | ± 10.4      | -     |  |
| Gender categorical                                 |             |       |  |
| Units: Subjects                                    |             |       |  |
| Female   | 2           | 2     |  |
| Male   | 31          | 31    |  |

## End points

### End points reporting groups

|   |                                   |
|---|-----------------------------------|
| Reporting group title   | flush model                       |
| Reporting group description:<br>The period 1 (1 week) includes cross-over (first and third sessions) and split face design (second session). During this period, the study drugs are applied as follows:<br>placebo gel on both sides on face;<br>one side of the face treated with CD07805/47 0.5% gel and the other side with CD07805/47 placebo gel (allocation of treatment on each half-face is randomized)<br>CD07805/47 0.5% gel on both sides on face |                                   |
| Reporting group title   | CD07805/47 0.5% gel cross over    |
| Reporting group description:<br>The period 2 (4 weeks) corresponds to a cross-over design. The CD07805/47 0.5% gel is applied once a day on the whole face and then the CD07805/47 placebo gel for the 2 following weeks or inversely according to randomisation  |                                   |
| Reporting group title   | CD07805/47 Placebo gel cross-over |
| Reporting group description:<br>The period 2 (4 weeks) corresponds to a cross-over design. The CD07805/47 0.5% gel is applied once a day on the whole face and then the CD07805/47 placebo gel for the 2 following weeks or inversely according to randomization  |                                   |

### Primary: total number of flushes for each 2-week period in Period 2

|   |  |
|---|--|
| End point title   | total number of flushes for each 2-week period in Period 2 |
| End point description:<br>The primary efficacy endpoint of this study was the total number of flushes reported in the subject diary for each 2-week period in Period 2. |  |
| End point type  | Primary  |
| End point timeframe:<br>Day 22 Day 36/Early termination   |  |

| End point values                     | CD07805/47 0.5% gel cross over | CD07805/47 Placebo gel cross-over |  |  |
|--------------------------------------|--------------------------------|-----------------------------------|--|--|
| Subject group type                   | Reporting group                | Reporting group                   |  |  |
| Number of subjects analysed          | 31 <sup>[1]</sup>              | 31 <sup>[2]</sup>                 |  |  |
| Units: flushes count                 |                                |                                   |  |  |
| arithmetic mean (standard deviation) | 15.3 (± 12.1)                  | 16.3 (± 14)                       |  |  |

Notes:

[1] - One subject was excluded from ITT (Intent to treat) population (no efficacy assessment performed)

[2] - One subject was excluded from ITT (Intent to treat) population (no efficacy assessment performed)

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title  | CD07805/47 0.5% gel vs CD07805/47 Placebo gel                      |
| Statistical analysis description:<br>31 subjects were in this analysis based on 62 values |  |
| Comparison groups   | CD07805/47 0.5% gel cross over v CD07805/47 Placebo gel cross-over |



|   |                        |
|---|------------------------|
| Number of subjects included in analysis | 62                     |
| Analysis specification                  | Pre-specified          |
| Analysis type                           | superiority            |
| P-value                                 | = 0.742 <sup>[3]</sup> |
| Method                                  | ANOVA                  |

Notes:

[3] - P value associated to treatment effect in the model. Study design with a power of 80% and a type I error at 5 % (two-sided)

Analysis of variance including sequence, subject (sequence), period and treatment as factor in the model.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The collection of AEs is from the time that a subject signs the ICF to their final visit. Adverse event reporting additional description:

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 16.0   |

### Reporting groups

|                                |                            |
|--------------------------------|----------------------------|
| Reporting group title          | Split Face design Period 1 |
| Reporting group description: - |                            |
| Reporting group title          | Cross over design period 1 |
| Reporting group description: - |                            |
| Reporting group title          | Cross-over design Period 2 |
| Reporting group description: - |                            |

| Serious adverse events                            | Split Face design Period 1 | Cross over design period 1 | Cross-over design Period 2 |
|---|----------------------------|----------------------------|----------------------------|
| Total subjects affected by serious adverse events |                            |                            |                            |
| subjects affected / exposed                       | 0 / 33 (0.00%)             | 0 / 34 (0.00%)             | 0 / 32 (0.00%)             |
| number of deaths (all causes)                     | 0                          | 0                          | 0                          |
| number of deaths resulting from adverse events    | 0                          | 0                          | 0                          |

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

| Non-serious adverse events                            | Split Face design Period 1   | Cross over design period 1 | Cross-over design Period 2 |
|---|--|----------------------------|----------------------------|
| Total subjects affected by non-serious adverse events |  |                            |                            |
| subjects affected / exposed                           | 2 / 33 (6.06%)   | 1 / 34 (2.94%)             | 5 / 32 (15.63%)            |
| Nervous system disorders                              |  |                            |                            |
| Headache  | Additional description: non cutaneous adverse event                      |                            |                            |
| subjects affected / exposed                           | 0 / 33 (0.00%)   | 0 / 34 (0.00%)             | 1 / 32 (3.13%)             |
| occurrences (all)                                     | 0  | 0                          | 1                          |
| Eye disorders   |  |                            |                            |
| erythema of eyelid                                    | Additional description: Adverse event not related to CD07805/47 0,5% gel |                            |                            |
| subjects affected / exposed                           | 0 / 33 (0.00%)   | 0 / 34 (0.00%)             | 1 / 32 (3.13%)             |
| occurrences (all)                                     | 0  | 0                          | 1                          |
| Gastrointestinal disorders                            |  |                            |                            |

|   |   |                |                |
|---|---|----------------|----------------|
| Cheilitis<br>subjects affected / exposed<br>occurrences (all)   | Additional description: Adverse event not related to CD07805 0.5% gel   |                |                |
|   | 0 / 33 (0.00%)  | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
|   | 0   | 0              | 1              |
| Oral herpes<br>subjects affected / exposed<br>occurrences (all)   | Additional description: Adverse event not related to CD07805/47 0.5% gel  |                |                |
|   | 0 / 33 (0.00%)  | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
|   | 0   | 0              | 1              |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)   | Additional description: Non cutaneous adverse event   |                |                |
|   | 0 / 33 (0.00%)  | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
|   | 0   | 0              | 1              |
| Skin and subcutaneous tissue disorders<br>erythema and skin tightness<br>subjects affected / exposed<br>occurrences (all) |   |                |                |
|   | Additional description: cutaneous adverse event related to CD07805/47 0.5% gel  |                |                |
|   | 0 / 33 (0.00%)  | 1 / 34 (2.94%) | 0 / 32 (0.00%) |
|   | 0   | 2              | 0              |
| erythema, papules and pruritus<br>subjects affected / exposed<br>occurrences (all)  | Additional description: During the split face design period 1, cutaneous adverse events were related to CD07805 placebo gel<br>During the cross over design period 2, adverse events of special interest were related to CD07805/47 0.5% gel leading to subject discontinuation |                |                |
|   | 2 / 33 (6.06%)  | 0 / 34 (0.00%) | 1 / 32 (3.13%) |
|   | 6   | 0              | 3              |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### 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.

|               |
|---------------|
| none reported |
|---------------|

Notes: