



## Clinical trial results:

**Multi-centre, randomized, double-blind trial to compare the efficacy and safety of tretinoin clindamycin phosphate gel to clindamycin phosphate gel alone in the treatment of acne vulgaris in patients from 12 to less than 18 years of age.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2010-022919-20 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 01 March 2006  |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 29 July 2016 |
| First version publication date | 29 July 2016 |

### Trial information

#### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | MP-1501-02 |
|-----------------------|------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Dow Pharmaceutical Sciences, Inc.   |
| Sponsor organisation address | 1330A Redwood Way, Petaluma, United States, CA 94954-1169   |
| Public contact               | Group leader study manager, MEDA Pharma GmbH & Co. KG, +49 617288801, 42b@medapharma.de           |
| Scientific contact           | Head of Corporate Clinical Affairs, MEDA Pharma GmbH & Co. KG, +49 617288801, 42b@medapharma.de   |
| Sponsor organisation name    | Medicis Pharmaceutical Corp.  |
| Sponsor organisation address | 8125 North Hayden Road, Scottsdale, United States, AZ 85258                                       |
| Public contact               | Group leader study manager, Meda Pharma GmbH & Co. KG, +49 6172 888 01, 42b@medapharma.de         |
| Scientific contact           | Head of Corporate Clinical Affairs, Meda Pharma GmbH & Co. KG, +49 6172 888 01, 42b@medapharma.de |

Notes:

### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes                 |
| EMA paediatric investigation plan number(s)                    | EMA-000892-PIP01-10 |
| Does article 45 of REGULATION (EC) No                          | Yes                 |

|  |    |
|--|----|
| 1901/2006 apply to this trial?                                       |    |
| 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                       | 21 April 2006 |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 01 March 2006 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 01 March 2006 |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

To compare the efficacy and safety of Clin-RA Gel to Clindamycin phosphate 1.2% gel alone in the treatment of acne vulgaris.

Protection of trial subjects:

No specific additional measures to minimise pain and distress were required. The subjects could withdraw from treatment at any time and for any reason.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 09 September 2005 |
| 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 | United States: 2010 |
| Worldwide total number of subjects   | 2010                |
| EEA total number of subjects         | 0                   |

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)                 | 1320 |

|                      |     |
|----------------------|-----|
| Adults (18-64 years) | 689 |
| From 65 to 84 years  | 1   |
| 85 years and over    | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Male or female subjects of any race, 12 years of age or older, with acne vulgaris, with 20 to 50 inflammatory lesions (papules and pustules), 20 to 100 noninflammatory lesions (open and closed comedones), no more than 2 nodules, and an Evaluator's Global Severity Score (EGSS) of moderate (=3) or severe (=4).

### 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, Carer, Assessor |

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | Clin RA Gel |

Arm description: -

|  |   |
|--|---|
| Arm type                               | Experimental                                    |
| Investigational medicinal product name | Clindamycin phosphate 1.2% and tretinoin 0.025% |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Gel   |
| Routes of administration               | Topical use                                     |

Dosage and administration details:

once-a-day application (at bedtime); topically applied to the face

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | Clindamycin |
|------------------|-------------|

Arm description: -

|  |                            |
|--|----------------------------|
| Arm type                               | Active comparator          |
| Investigational medicinal product name | Clindamycin phosphate 1.2% |
| Investigational medicinal product code |                            |
| Other name                             |                            |
| Pharmaceutical forms                   | Gel                        |
| Routes of administration               | Topical use                |

Dosage and administration details:

once-a-day application (at bedtime); topically applied to the face

| Number of subjects in period 1 | Clin RA Gel | Clindamycin |
|--------------------------------|-------------|-------------|
| Started                        | 1008        | 1002        |
| Completed                      | 859         | 838         |
| Not completed                  | 149         | 164         |
| Consent withdrawn by subject   | 27          | 20          |
| Adverse event, non-fatal       | 6           | 2           |

|                    |    |     |
|--------------------|----|-----|
| Other              | 5  | 3   |
| Subject request    | 17 | 28  |
| Lost to follow-up  | 92 | 108 |
| Protocol deviation | 1  | -   |
| Noncompliance      | 1  | 3   |

## Baseline characteristics

### Reporting groups

|                                |             |
|--------------------------------|-------------|
| Reporting group title          | Clin RA Gel |
| Reporting group description: - |             |
| Reporting group title          | Clindamycin |
| Reporting group description: - |             |

| Reporting group values                                | Clin RA Gel | Clindamycin | Total |
|---|-------------|-------------|-------|
| Number of subjects                                    | 1008        | 1002        | 2010  |
| Age categorical<br>Units: Subjects                    |             |             |       |
| In utero  |             |             | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) |             |             | 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)                                  |             |             | 0     |
| From 65-84 years                                      |             |             | 0     |
| 85 years and over                                     |             |             | 0     |
| Age continuous<br>Units: years                        |             |             |       |
| arithmetic mean                                       | 19.1        | 19          |       |
| standard deviation                                    | ± 7.5       | ± 7         | -     |
| Gender categorical<br>Units: Subjects                 |             |             |       |
| Female  | 493         | 547         | 1040  |
| Male  | 515         | 455         | 970   |

## End points

### End points reporting groups

|                                |             |
|--------------------------------|-------------|
| Reporting group title          | Clin RA Gel |
| Reporting group description: - |             |
| Reporting group title          | Clindamycin |
| Reporting group description: - |             |

### Primary: Dichotomized Evaluator's Global Severity Score

|                        |  |
|------------------------|--|
| End point title        | Dichotomized Evaluator's Global Severity Score |
| End point description: |  |
| End point type         | Primary  |
| End point timeframe:   |  |
| Baseline and week 12.  |  |

| End point values            | Clin RA Gel     | Clindamycin     |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 1008            | 1002            |  |  |
| Units: Success, Failure     |                 |                 |  |  |
| Success                     | 381             | 318             |  |  |
| Failure                     | 627             | 684             |  |  |

### Statistical analyses

|   |                           |
|---|---------------------------|
| Statistical analysis title              | Clin-RA vs Clindamycin    |
| Comparison groups                       | Clin RA Gel v Clindamycin |
| Number of subjects included in analysis | 2010                      |
| Analysis specification                  | Pre-specified             |
| Analysis type                           | superiority               |
| P-value                                 | = 0.002                   |
| Method                                  | Cochran-Mantel-Haenszel   |

### Primary: Percent Change from Baseline in Inflammatory Lesion Count / Week 12

|                        |   |
|------------------------|---|
| End point title        | Percent Change from Baseline in Inflammatory Lesion Count / Week 12 |
| End point description: |   |
| End point type         | Primary   |

End point timeframe:  
Baseline and week 12.

|                               |                    |                      |  |  |
|-------------------------------|--------------------|----------------------|--|--|
| <b>End point values</b>       | Clin RA Gel        | Clindamycin          |  |  |
| Subject group type            | Reporting group    | Reporting group      |  |  |
| Number of subjects analysed   | 1008               | 1002                 |  |  |
| Units: percent change         |                    |                      |  |  |
| median (full range (min-max)) | 70 (-215.6 to 100) | 64.5 (-146.4 to 100) |  |  |

### Statistical analyses

|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>       | Clin-RA vs Clindamycin    |
| Comparison groups                       | Clin RA Gel v Clindamycin |
| Number of subjects included in analysis | 2010                      |
| Analysis specification                  | Pre-specified             |
| Analysis type                           | superiority               |
| P-value                                 | < 0.001                   |
| Method                                  | Cochran-Mantel-Haenszel   |

### Primary: Percent Change from Baseline in Non-inflammatory Lesion Count / Week 12

|   |   |
|---|---|
| End point title                               | Percent Change from Baseline in Non-inflammatory Lesion Count / Week 12 |
| End point description:                        |   |
| End point type                                | Primary   |
| End point timeframe:<br>Baseline and week 12. |   |

|                               |                      |                      |  |  |
|-------------------------------|----------------------|----------------------|--|--|
| <b>End point values</b>       | Clin RA Gel          | Clindamycin          |  |  |
| Subject group type            | Reporting group      | Reporting group      |  |  |
| Number of subjects analysed   | 1008                 | 1002                 |  |  |
| Units: percent change         |                      |                      |  |  |
| median (full range (min-max)) | 57.6 (-157.8 to 100) | 48.2 (-184.6 to 100) |  |  |

### Statistical analyses



|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>       | Clin-RA vs Clindamycin    |
| Comparison groups                       | Clin RA Gel v Clindamycin |
| Number of subjects included in analysis | 2010                      |
| Analysis specification                  | Pre-specified             |
| Analysis type                           | superiority               |
| P-value                                 | < 0.001                   |
| Method                                  | Cochran-Mantel-Haenszel   |

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**Primary: Percent Change from Baseline in Total Lesion Count / Week 12**

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|                        |  |
|------------------------|--|
| End point title        | Percent Change from Baseline in Total Lesion Count / Week 12 |
| End point description: |  |
| End point type         | Primary  |
| End point timeframe:   |  |
| Baseline and week 12.  |  |

|                               |                   |                      |  |  |
|-------------------------------|-------------------|----------------------|--|--|
| <b>End point values</b>       | Clin RA Gel       | Clindamycin          |  |  |
| Subject group type            | Reporting group   | Reporting group      |  |  |
| Number of subjects analysed   | 1008              | 1002                 |  |  |
| Units: percent change         |                   |                      |  |  |
| median (full range (min-max)) | 62 (-97.4 to 100) | 53.1 (-107.4 to 100) |  |  |

**Statistical analyses**

|   |                           |
|---|---------------------------|
| <b>Statistical analysis title</b>       | Clin-RA vs Clindamycin    |
| Comparison groups                       | Clin RA Gel v Clindamycin |
| Number of subjects included in analysis | 2010                      |
| Analysis specification                  | Pre-specified             |
| Analysis type                           | superiority               |
| P-value                                 | < 0.001                   |
| Method                                  | Cochran-Mantel-Haenszel   |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:  
during 12 weeks of treatment, until 30 days post-treatment

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

### Dictionary used

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

|                    |     |
|--------------------|-----|
| Dictionary version | 8.1 |
|--------------------|-----|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Clindamycin |
|-----------------------|-------------|

Reporting group description:

Clindamycin phosphate 1.2% gel (in the same vehicle as the investigational product); once-a-day application (at bedtime); topically applied to the face

|                       |             |
|-----------------------|-------------|
| Reporting group title | Clin RA Gel |
|-----------------------|-------------|

Reporting group description:

Clindamycin phosphate 1.2% and tretinoin 0.025% once-a-day application (at bedtime); topically applied to the face

| Serious adverse events                            | Clindamycin      | Clin RA Gel      |  |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events |                  |                  |  |
| subjects affected / exposed                       | 3 / 1002 (0.30%) | 2 / 1008 (0.20%) |  |
| number of deaths (all causes)                     | 0                | 0                |  |
| number of deaths resulting from adverse events    | 0                | 0                |  |
| Congenital, familial and genetic disorders        |                  |                  |  |
| Dermoid cyst                                      |                  |                  |  |
| subjects affected / exposed                       | 1 / 1002 (0.10%) | 0 / 1008 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Surgical and medical procedures                   |                  |                  |  |
| Abdominoplasty                                    |                  |                  |  |
| subjects affected / exposed                       | 1 / 1002 (0.10%) | 0 / 1008 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |
| Psychiatric disorders                             |                  |                  |  |
| Depression  |                  |                  |  |
| subjects affected / exposed                       | 0 / 1002 (0.00%) | 1 / 1008 (0.10%) |  |
| occurrences causally related to treatment / all   | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all        | 0 / 0            | 0 / 0            |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Intentional selfinjury                          |                  |                  |  |
| subjects affected / exposed                     | 0 / 1002 (0.00%) | 1 / 1008 (0.10%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Infections and infestations                     |                  |                  |  |
| Tonsillitis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1002 (0.10%) | 0 / 1008 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |

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

| <b>Non-serious adverse events</b>                     | Clindamycin         | Clin RA Gel         |  |
|---|---------------------|---------------------|--|
| Total subjects affected by non-serious adverse events |                     |                     |  |
| subjects affected / exposed                           | 235 / 1002 (23.45%) | 269 / 1008 (26.69%) |  |
| Nervous system disorders                              |                     |                     |  |
| Headache  |                     |                     |  |
| subjects affected / exposed                           | 12 / 1002 (1.20%)   | 20 / 1008 (1.98%)   |  |
| occurrences (all)                                     | 12                  | 20                  |  |
| Gastrointestinal disorders                            |                     |                     |  |
| Nausea  |                     |                     |  |
| subjects affected / exposed                           | 7 / 1002 (0.70%)    | 11 / 1008 (1.09%)   |  |
| occurrences (all)                                     | 7                   | 11                  |  |
| Respiratory, thoracic and mediastinal disorders       |                     |                     |  |
| Pharyngolaryngeal pain                                |                     |                     |  |
| subjects affected / exposed                           | 16 / 1002 (1.60%)   | 19 / 1008 (1.88%)   |  |
| occurrences (all)                                     | 16                  | 19                  |  |
| Cough   |                     |                     |  |
| subjects affected / exposed                           | 15 / 1002 (1.50%)   | 12 / 1008 (1.19%)   |  |
| occurrences (all)                                     | 15                  | 12                  |  |
| Skin and subcutaneous tissue disorders                |                     |                     |  |
| Dry skin  |                     |                     |  |
| subjects affected / exposed                           | 7 / 1002 (0.70%)    | 20 / 1008 (1.98%)   |  |
| occurrences (all)                                     | 7                   | 20                  |  |
| Infections and infestations                           |                     |                     |  |

|                                   |                   |                   |  |
|-----------------------------------|-------------------|-------------------|--|
| Nasopharyngitis                   |                   |                   |  |
| subjects affected / exposed       | 54 / 1002 (5.39%) | 51 / 1008 (5.06%) |  |
| occurrences (all)                 | 54                | 51                |  |
| Upper respiratory tract infection |                   |                   |  |
| subjects affected / exposed       | 17 / 1002 (1.70%) | 12 / 1008 (1.19%) |  |
| occurrences (all)                 | 17                | 12                |  |
| Pharyngitis streptococcal         |                   |                   |  |
| subjects affected / exposed       | 12 / 1002 (1.20%) | 9 / 1008 (0.89%)  |  |
| occurrences (all)                 | 12                | 9                 |  |
| Sinusitis                         |                   |                   |  |
| subjects affected / exposed       | 14 / 1002 (1.40%) | 12 / 1008 (1.19%) |  |
| occurrences (all)                 | 14                | 12                |  |
| Influenza                         |                   |                   |  |
| subjects affected / exposed       | 7 / 1002 (0.70%)  | 11 / 1008 (1.09%) |  |
| occurrences (all)                 | 7                 | 11                |  |
| Gastroenteritis viral             |                   |                   |  |
| subjects affected / exposed       | 11 / 1002 (1.10%) | 9 / 1008 (0.89%)  |  |
| occurrences (all)                 | 11                | 9                 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date           | Amendment   |
|----------------|---|
| 17 August 2005 | Implemented changes to study procedures and analyses requested by the FDA |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported