Clinical trial results:
A Multi-centre, Open-label, Long-term, Safety Trial of Clin RA Gel in the Treatment of Acne Vulgaris.

Summary

EudraCT number	2010-022912-37
Trial protocol	Outside EU/EEA
Global end of trial date	21 January 2005

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-1501-01

Additional study identifiers

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

Notes:

Sponsors

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
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 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)	EMEA-000892-PIP01-10
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	11 April 2006
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 January 2005
Global end of trial reached?	Yes
Global end of trial date	21 January 2005
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the long-term safety of the new combination therapy as a single therapy or with other concomitant acne medications for a six month period or one year period.

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	23 January 2004
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: 442
Worldwide total number of subjects	442
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)	242
Adults (18-64 years)	200
From 65 to 84 years	0

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 mild, moderate, or severe acne vulgaris.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Cohort 1

Arm description:

Cohort 1 consists of all subjects who entered the long-term study and are the population of subjects in the 0 to 6 Month analyses.

Arm type	Experimental
Investigational medicinal product name	Clin RA Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Topical application of study drug (active ingredients: Clindamycin phosphate 1.2% and Tretinoin 0.025%) was made to the face once daily prior to bedtime, as directed by the investigator. After cleansing, the study drug was applied as a thin coating and rubbed into the skin. Total weekly dosage of study drug was anticipated to be no more than approximately 5 g/week.

Arm title	Cohort 2

Arm description:

Cohort 2 consists of those subjects in Cohort 1 who continued to participate in the study past their 6-month visit and are the population of subjects in the 7 to 12-month analyses.

Arm type	Experimental
Investigational medicinal product name	Clin RA Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Topical application of study drug (active ingredients: Clindamycin phosphate 1.2% and Tretinoin 0.025%) was made to the face once daily prior to bedtime, as directed by the investigator. After cleansing, the study drug was applied as a thin coating and rubbed into the skin. Total weekly dosage of study drug was anticipated to be no more than approximately 5 g/week.

Number of subjects in period 1	Cohort 1	Cohort 2
Started	442	213
Completed	352	195
Not completed	90	18
Acne flair	1	-
Adverse event, non-fatal	3	-
Not reported	-	2
Subject request	40	8
Lost to follow-up	44	7
Protocol deviation	1	-
Investigator request	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
Cohort 1 consists of all subjects who entered the long-term study and are the population of subjects in the 0 to 6 Month analyses.	
Reporting group title	Cohort 2
Reporting group description:	
Cohort 2 consists of those subjects in Cohort 1 who continued to participate in the study past their 6-month visit and are the population of subjects in the 7 to 12-month analyses.	

Reporting group values	Cohort 1	Cohort 2	Total
Number of subjects	442	213	442
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	20.4	20.16	
standard deviation	± 8.41	± 8.27	-
Gender categorical Units: Subjects			
Female	263	128	263
Male	179	85	179
Evaluator's Global Severity Score at Baseline Units: Subjects			
Clear	0	0	0
Almost Clear	0	0	0
Mild	217	106	217
Moderate	166	79	166
Severe	59	28	59
Very Severe	0	0	0

End points

End points reporting groups

Reporting group title	Cohort 1

Reporting group description:

Cohort 1 consists of all subjects who entered the long-term study and are the population of subjects in the 0 to 6 Month analyses.

Reporting group title	Cohort 2

Reporting group description:

Cohort 2 consists of those subjects in Cohort 1 who continued to participate in the study past their 6-month visit and are the population of subjects in the 7 to 12-month analyses.

Primary: Evaluator's Global Severity Score at Month 1

End point title	Evaluator's Global Severity Score at Month 1[1][2]

End point description:

End point type	Primary

End point timeframe:

Month 1 after baseline.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 1.

End point values	Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	424[3]			
Units: subjects				
Clear	0			
Almost Clear	34			
Mild	237			
Moderate	134			
Severe	16			
Very Severe	1			
Not Reported	2			

Notes:

[3] - 424 subjects available at month 1.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 2

End point title	Evaluator's Global Severity Score at Month 2[4][5]

End point description:

End point type	Primary

End point timeframe:

Month 2 after baseline.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 1.

End point values	Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	395[6]			
Units: subjects				
Clear	6			
Almost Clear	87			
Mild	211			
Moderate	86			
Severe	5			
Very Severe	0			
Not Reported	0			

Notes:

[6] - 395 subjects avalibale at month 2.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 3

End point title	Evaluator's Global Severity Score at Month 3[7][8]

End point description:

End point type	Primary

End point timeframe:

Month 3 after baseline.

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 1.

End point values	Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	384[9]			
Units: subjects				
Clear	19			
Almost Clear	108			
Mild	179			
Moderate	76			

Severe	2			
Very Severe	0			
Not Reported	0			

Notes:

[9] - 384 subjects avaliable at month 3.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 4

End point title	Evaluator's Global Severity Score at Month 4[10][11]

End point description:

End point type	Primary

End point timeframe:

Month 4 after baseline.

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 1.

End point values	Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	367[12]			
Units: subjects				
Clear	20			
Almost Clear	129			
Mild	154			
Moderate	63			
Severe	1			
Very Severe	0			
Not Reported	0			

Notes:

[12] - 367 subjects available at month 4.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 5

End point title	Evaluator's Global Severity Score at Month 5[13][14]

End point description:

End point type	Primary

End point timeframe:

Month 5 after baseline.

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 1.

End point values	Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	354[15]			
Units: subjects				
Clear	24			
Almost Clear	133			
Mild	138			
Moderate	58			
Severe	1			
Very Severe	0			
Not Reported	0			

Notes:

[15] - 354 subjects available at month 5.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 6

End point title	Evaluator's Global Severity Score at Month 6[16][17]

End point description:

End point type	Primary

End point timeframe:

Month 6 after baseline.

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 1.

End point values	Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	351[18]			
Units: subjects				
Clear	32			
Almost Clear	124			
Mild	132			
Moderate	60			
Severe	3			
Very Severe	0			

Not Reported	0			

Notes:

[18] - 351 subjects available at month 6.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 7

End point title	Evaluator's Global Severity Score at Month 7[19][20]

End point description:

End point type	Primary

End point timeframe:

Month 7 after baseline.

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 2.

End point values	Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	206[21]			
Units: subjects				
Clear	17			
Almost Clear	77			
Mild	82			
Moderate	28			
Severe	2			
Very Severe	0			
Not Reported	0			

Notes:

[21] - 206 subjects available at month 7.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 8

End point title	Evaluator's Global Severity Score at Month 8[22][23]

End point description:

End point type	Primary

End point timeframe:

Month 8 after baseline.

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 2.

End point values	Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	200[24]			
Units: subjects				
Clear	23			
Almost Clear	68			
Mild	76			
Moderate	32			
Severe	0			
Very Severe	0			
Not Reported	1			

Notes:

[24] - 200 subjects available at month 8.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 9

End point title	Evaluator's Global Severity Score at Month 9[25][26]

End point description:

End point type	Primary

End point timeframe:

Month 9 after baseline.

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 2.

End point values	Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	201[27]			
Units: subjects				
Clear	17			
Almost Clear	80			
Mild	72			
Moderate	30			
Severe	2			
Very Severe	0			

Not Reported	0			

Notes:

[27] - 201 subjects available at month 9.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 10

End point title	Evaluator's Global Severity Score at Month 10[28][29]

End point description:

End point type	Primary

End point timeframe:

Month 10 after baseline.

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 2.

End point values	Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	198[30]			
Units: subjects				
Clear	16			
Almost Clear	81			
Mild	74			
Moderate	24			
Severe	3			
Very Severe	0			
Not Reported	0			

Notes:

[30] - 198 subjects available at month 10.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 11

End point title	Evaluator's Global Severity Score at Month 11[31][32]

End point description:

End point type	Primary

End point timeframe:

Month 11 after baseline.

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 2.

End point values	Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	196[33]			
Units: subjects				
Clear	22			
Almost Clear	75			
Mild	69			
Moderate	29			
Severe	1			
Very Severe	0			
Not Reported	0			

Notes:

[33] - 196 subjects available at month 11.

Statistical analyses

No statistical analyses for this end point

Primary: Evaluator's Global Severity Score at Month 12

End point title	Evaluator's Global Severity Score at Month 12[34][35]

End point description:

End point type	Primary

End point timeframe:

Month 12 after baseline.

Notes:

[34] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No other statistical analyses besides descriptive statistics available for this end point.

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This end point reports only statistics for the arm Cohort 2.

End point values	Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	195[36]			
Units: subjects				
Clear	36			
Almost Clear	76			
Mild	62			
Moderate	18			
Severe	3			
Very Severe	0			

Not Reported	0			

Notes:

[36] - 195 subjects available at month 12.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Study duration.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	7.0
Reporting groups	
Reporting group title	Safety Evaluable Population

Reporting group description: -

Serious adverse events	Safety Evaluable Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 442 (1.36%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Surgical and medical procedures			
Bunion operation			
subjects affected / exposed	1 / 442 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystectomy			
subjects affected / exposed	1 / 442 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Eclampsia			
subjects affected / exposed	1 / 442 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Caesarean section			
subjects affected / exposed	1 / 442 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 442 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 442 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 442 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 442 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0.5 %

Non-serious adverse events	Safety Evaluable Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	197 / 442 (44.57%)		
Injury, poisoning and procedural complications			
Sunburn			
subjects affected / exposed	12 / 442 (2.71%)		
occurrences (all)	12		
Road traffic accident			
subjects affected / exposed	5 / 442 (1.13%)		
occurrences (all)	5		
Joint sprain			
subjects affected / exposed	3 / 442 (0.68%)		
occurrences (all)	3		
Post procedural pain			

subjects affected / exposed occurrences (all)	3 / 442 (0.68%) 3		
Surgical and medical procedures Wisdom teeth removal subjects affected / exposed occurrences (all)	 3 / 442 (0.68%) 3		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Sinus headache subjects affected / exposed occurrences (all)	 21 / 442 (4.75%) 21 3 / 442 (0.68%) 3		
General disorders and administration site conditions Application site dermatitis subjects affected / exposed occurrences (all) Application site desquamation subjects affected / exposed occurrences (all) Application site dryness subjects affected / exposed occurrences (all)	 3 / 442 (0.68%) 3 3 / 442 (0.68%) 3 3 / 442 (0.68%) 3		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all) Seasonal allergy subjects affected / exposed occurrences (all)	 7 / 442 (1.58%) 7 3 / 442 (0.68%) 3		
Gastrointestinal disorders Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) Toothache	 5 / 442 (1.13%) 5 		

subjects affected / exposed occurrences (all)	3 / 442 (0.68%) 3		
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	 3 / 442 (0.68%) 3		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Pharyngolaryngeal pain subjects affected / exposed occurrences (all)	 6 / 442 (1.36%) 6 3 / 442 (0.68%) 3		
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) Dermatitis contact subjects affected / exposed occurrences (all) Photosensitivity reaction subjects affected / exposed occurrences (all)	 29 / 442 (6.56%) 29 5 / 442 (1.13%) 5 3 / 442 (0.68%) 3		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	 3 / 442 (0.68%) 3		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 6 / 442 (1.36%) 6		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis	 17 / 442 (3.85%) 17		

subjects affected / exposed	13 / 442 (2.94%)			
occurrences (all)	13			
Ear infection				
subjects affected / exposed	3 / 442 (0.68%)			
occurrences (all)	3			
Bronchitis				
subjects affected / exposed	4 / 442 (0.90%)			
occurrences (all)	4			
Gastroenteritis viral				
subjects affected / exposed	6 / 442 (1.36%)			
occurrences (all)	6			
Fungal infection				
subjects affected / exposed	3 / 442 (0.68%)			
occurrences (all)	3			
Pharyngitis				
subjects affected / exposed	3 / 442 (0.68%)			
occurrences (all)	3			
Pharyngitis streptococcal				
subjects affected / exposed	3 / 442 (0.68%)			
occurrences (all)	3			
Rhinitis				
subjects affected / exposed	4 / 442 (0.90%)			
occurrences (all)	4			
Viral infection				
subjects affected / exposed	3 / 442 (0.68%)			
occurrences (all)	3			
Tooth infection				
subjects affected / exposed	3 / 442 (0.68%)			
occurrences (all)	3			
Gastroenteritis				
subjects affected / exposed	5 / 442 (1.13%)			
occurrences (all)	5			
Upper respiratory tract infection				
subjects affected / exposed	33 / 442 (7.47%)			
occurrences (all)	33			
Urinary tract infection				

subjects affected / exposed occurrences (all)	4 / 442 (0.90%) 4		

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