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

Summary

EudraCT number	2010-022918-15
Trial protocol	Outside EU/EEA
Global end of trial date	21 October 2003

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	7001-G2HP-07-02

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dow Pharmaceutical Sciences
Sponsor organisation address	127 Hospital Drive, #202, Vallejo, United States, CA 94589
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	28 January 2004
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 October 2003
Global end of trial reached?	Yes
Global end of trial date	21 October 2003
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, Tretinoin 0.025% Gel alone, and Clin-RA Gel vehicle 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	11 February 2003
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: 1288
Worldwide total number of subjects	1288
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)	2
Adolescents (12-17 years)	793
Adults (18-64 years)	493
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 acne vulgaris, presenting with 20-50 inflammatory lesions (papules and pustules), 20-100 non-inflammatory lesions (open and closed comedones), and < 2 nodules.

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	Clin-RA

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:

Clin-RA Gel (Clindamycin phosphate 1.2% and Tretinoin 0.025%)
Dosing: Once-a-day application (at bedtime)
Mode of Administration: Topically applied to the face

Arm title	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:

Clindamycin phosphate 1.2% (in same vehicle as investigational product)
Dosing: Once-a-day application (at bedtime)
Mode of Administration: Topically applied to the face

Arm title	Tretinoin

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Tretinoin 0.025%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Tretinoin 0.025% (in same vehicle as investigational product)
Dosing: Once-a-day application (at bedtime)
Mode of Administration: Topically applied to the face

Arm title	Vehicle
Arm description: -	
Arm type	Vehicle
Investigational medicinal product name	N/A (vehicle)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Dosing: Once-a-day application (at bedtime)
Mode of Administration: Topically applied to the face

Number of subjects in period 1	Clin-RA	Clindamycin	Tretinoin
Started	425	218	429
Completed	352	183	347
Not completed	73	35	82
Adverse event, non-fatal	5	1	3
Other	3	2	5
Inappropriate enrollment	1	1	2
Subject request	27	11	21
Lost to follow-up	29	18	33
Pregnancy	-	-	2
Protocol deviation	3	-	6
Lack of efficacy	5	2	10

Number of subjects in period 1	Vehicle
Started	216
Completed	173
Not completed	43
Adverse event, non-fatal	1
Other	3
Inappropriate enrollment	2
Subject request	14
Lost to follow-up	15
Pregnancy	-
Protocol deviation	1
Lack of efficacy	7

Baseline characteristics

Reporting groups	
Reporting group title	Clin-RA
Reporting group description: -	
Reporting group title	Clindamycin
Reporting group description: -	
Reporting group title	Tretinoin
Reporting group description: -	
Reporting group title	Vehicle
Reporting group description: -	

Reporting group values	Clin-RA	Clindamycin	Tretinoin
Number of subjects	425	218	429
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	19.22	19.25	19.38
standard deviation	± 8.01	± 8.11	± 8.14
Gender categorical Units: Subjects			
Female	235	111	236
Male	190	107	193

Reporting group values	Vehicle	Total	
Number of subjects	216	1288	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (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 Units: years			
arithmetic mean	19.04		
standard deviation	± 7.82	-	
Gender categorical Units: Subjects			
Female	110	692	
Male	106	596	

End points

End points reporting groups	
Reporting group title	Clin-RA
Reporting group description: -	
Reporting group title	Clindamycin
Reporting group description: -	
Reporting group title	Tretinoin
Reporting group description: -	
Reporting group title	Vehicle
Reporting group description: -	

Primary: Dichotomized Evaluator's Global Severity Score / Week 12	
End point title	Dichotomized Evaluator's Global Severity Score / Week 12
End point description:	
End point type	Primary
End point timeframe: Week 12	

End point values	Clin-RA	Clindamycin	Tretinoin	Vehicle
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	425	218	429	216
Units: Success, Failure				
Success	95	38	60	16
Failure	330	180	369	200

Statistical analyses

Statistical analysis title	Clin-RA vs. Clindamycin
Comparison groups	Clin-RA v Clindamycin
Number of subjects included in analysis	643
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.122
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Clin-RA vs. Tretinoin
Comparison groups	Clin-RA v Tretinoin

Number of subjects included in analysis	854
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Cochran-Mantel-Haenszel

Statistical analysis title	Clin-RA vs. Vehicle
Comparison groups	Clin-RA v Vehicle
Number of subjects included in analysis	641
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
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

End point values	Clin-RA	Clindamycin	Tretinoin	Vehicle
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	425	218	429	216
Units: percent change				
median (full range (min-max))	61.3 (-425 to 100)	52.1 (-250 to 100)	50 (-164 to 100)	38.9 (-100 to 100)

Statistical analyses

Statistical analysis title	Clin-RA vs. Clindamycin
Comparison groups	Clin-RA v Clindamycin
Number of subjects included in analysis	643
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Ranked ANOVA

Statistical analysis title	Clin-RA vs. Tretinoin
Comparison groups	Tretinoin v Clin-RA
Number of subjects included in analysis	854
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Ranked ANOVA

Statistical analysis title	Clin-RA vs. Vehicle
Comparison groups	Clin-RA v Vehicle
Number of subjects included in analysis	641
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Ranked ANOVA

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:

Baseline and week 12.

End point values	Clin-RA	Clindamycin	Tretinoin	Vehicle
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	425	218	429	216
Units: percent change				
median (full range (min-max))	42.3 (-238 to 100)	32.2 (-195 to 100)	40 (-326 to 100)	24.2 (-198 to 100)

Statistical analyses

Statistical analysis title	Clin-RA vs. Clindamycin
Comparison groups	Clin-RA v Clindamycin

Number of subjects included in analysis	643
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.088
Method	Ranked ANOVA

Statistical analysis title	Clin-RA vs. Tretinoin
Comparison groups	Clin-RA v Tretinoin
Number of subjects included in analysis	854
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11
Method	Ranked ANOVA

Statistical analysis title	Clin-RA vs. Vehicle
Comparison groups	Clin-RA v Vehicle
Number of subjects included in analysis	641
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Ranked ANOVA

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

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.

End point values	Clin-RA	Clindamycin	Tretinoin	Vehicle
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	425	218	429	216
Units: percent change				
median (full range (min-max))	48.4 (-245 to 100)	40.9 (-117 to 98)	39.7 (-150 to 100)	25 (-164 to 100)

Statistical analyses

Statistical analysis title	Clin-RA vs. Clindamycin
Comparison groups	Clin-RA v Clindamycin
Number of subjects included in analysis	643
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018
Method	Ranked ANOVA

Statistical analysis title	Clin-RA vs. Tretinoin
Comparison groups	Clin-RA v Tretinoin
Number of subjects included in analysis	854
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Ranked ANOVA

Statistical analysis title	Clin-RA vs. Vehicle
Comparison groups	Clin-RA v Vehicle
Number of subjects included in analysis	641
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Ranked ANOVA

Adverse events

Adverse events information	
Timeframe for reporting adverse events: until 30 days post-treatment	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	6.1
Reporting groups	
Reporting group title	Clin RA Gel
Reporting group description: Clindamycin phosphate 1.2% and Tretinoin 0.025%	
Reporting group title	Tretinoin
Reporting group description: Tretinoin 0.025% (in same vehicle as investigational product)	
Reporting group title	Vehicle
Reporting group description: Clin-RA Gel Vehicle	
Reporting group title	Clindamycin
Reporting group description: Clindamycin phosphate 1.2% (in same vehicle as investigational product)	

Serious adverse events	Clin RA Gel	Tretinoin	Vehicle
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 425 (0.24%)	2 / 429 (0.47%)	2 / 216 (0.93%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 425 (0.00%)	0 / 429 (0.00%)	1 / 216 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 425 (0.00%)	1 / 429 (0.23%)	0 / 216 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholethiasis			

subjects affected / exposed	1 / 425 (0.24%)	0 / 429 (0.00%)	0 / 216 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour	Additional description: Hospitalization due to increase in behavior disorder		
subjects affected / exposed	0 / 425 (0.00%)	1 / 429 (0.23%)	1 / 216 (0.46%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Clindamycin		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 218 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholethiasis			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal behaviour	Additional description: Hospitalization due to increase in behavior disorder		
subjects affected / exposed	0 / 218 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Clin RA Gel	Tretinoin	Vehicle
Total subjects affected by non-serious adverse events			
subjects affected / exposed	117 / 425 (27.53%)	127 / 429 (29.60%)	46 / 216 (21.30%)
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 425 (1.88%)	8 / 429 (1.86%)	3 / 216 (1.39%)
occurrences (all)	8	8	3
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	10 / 425 (2.35%)	12 / 429 (2.80%)	3 / 216 (1.39%)
occurrences (all)	10	12	3
Cough			
subjects affected / exposed	2 / 425 (0.47%)	9 / 429 (2.10%)	0 / 216 (0.00%)
occurrences (all)	2	9	0
Nasopharyngitis			
subjects affected / exposed	7 / 425 (1.65%)	10 / 429 (2.33%)	3 / 216 (1.39%)
occurrences (all)	7	10	3
Pharyngolaryngeal pain			
subjects affected / exposed	6 / 425 (1.41%)	3 / 429 (0.70%)	5 / 216 (2.31%)
occurrences (all)	6	3	5
Sinusitis			
subjects affected / exposed	4 / 425 (0.94%)	9 / 429 (2.10%)	2 / 216 (0.93%)
occurrences (all)	4	9	2
Skin and subcutaneous tissue disorders			
Sunburn			
subjects affected / exposed	6 / 425 (1.41%)	11 / 429 (2.56%)	1 / 216 (0.46%)
occurrences (all)	6	11	1

Non-serious adverse events	Clindamycin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	59 / 218 (27.06%)		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 218 (2.75%)		
occurrences (all)	6		

Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	6 / 218 (2.75%)		
occurrences (all)	6		
Cough			
subjects affected / exposed	4 / 218 (1.83%)		
occurrences (all)	4		
Nasopharyngitis			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		
Pharyngolaryngeal pain			
subjects affected / exposed	0 / 218 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	2 / 218 (0.92%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Sunburn			
subjects affected / exposed	3 / 218 (1.38%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2003	Implemented changes to study procedures and analyses requested by the FDA

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported