



Clinical trial results:

A Multi-Center, Randomized, Double-Blind, Parallel-Group, Controlled Study to Assess the Efficacy, Safety and Tolerability of Oral DFD-29 Extended Release Capsules for the Treatment of Inflammatory Lesions of Rosacea over 16 weeks

Summary

EudraCT number	2016-003197-41
Trial protocol	DE
Global end of trial date	13 September 2018

Results information

Result version number	v1 (current)
This version publication date	27 March 2020
First version publication date	27 March 2020
Summary attachment (see zip file)	Protocol Synopsis (DFD-29-CD-002_CTP Amendment IV_2018-10-02_Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	DFD-29-CD-002
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dr. Reddy's Laboratories Inc.
Sponsor organisation address	8-2-337, Road No. 3 Banjara Hills, Hyderabad Telangana, Hyderabad, India, 500034
Public contact	Dr. Srinivas Sidgiddi, Dr. Reddy's Laboratories Inc., 0043 6649117209, srinivassidgiddi@drreddys.com
Scientific contact	Dr. Srinivas Sidgiddi, Dr. Reddy's Laboratories Inc., 001 9084585362, srinivassidgiddi@drreddys.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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 September 2018
Global end of trial reached?	Yes
Global end of trial date	13 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of oral DFD-29 (minocycline 20 mg and 40 mg capsules) in comparison to placebo in the treatment of inflammatory lesions of rosacea for 16 weeks.
To evaluate the safety and tolerability of oral DFD-29 (minocycline HCL 40mg capsules) in comparison to placebo in the treatment of inflammatory lesions of rosacea for 16 weeks.

Protection of trial subjects:

NA

Background therapy:

NA

Evidence for comparator:

Although there are multiple therapeutic options available for the treatment of papulopustular rosacea, the most widely used systemic agents are oral tetracycline derivatives, particularly doxycycline and minocycline. Oraycea® (doxycycline 40 mg capsules) was chosen as comparator as it has been approved in the US and the EU for the treatment of papulopustular rosacea.
A placebo group was required in order to differentiate any investigational drug effect from any improvement that could occur solely due to the close care and medical oversight given to patients under trial conditions.

Actual start date of recruitment	26 September 2017
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	Germany: 205
Worldwide total number of subjects	205
EEA total number of subjects	205

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	167
From 65 to 84 years	37
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

205 male and female subjects over the age of 18 diagnosed with papulopustular rosacea were recruited across 17 sites in Germany. First patient first visit occurred on 26 September 2017 and the last patient was recruited 10 July 2018.

Pre-assignment

Screening details:

Subjects had to be diagnosed with papulopustular rosacea, IGA grade 2 - 4 had to fulfill the following main criteria:

1. 10 - 40 (both inclusive) inflammatory lesions (papules and pustules) of rosacea over the face.
2. not more than 2 nodules
3. moderate to severe erythema with a total score of 5 - 20 on the CEA scale
4. good general health

Pre-assignment period milestones

Number of subjects started	219 ^[1]
Number of subjects completed	205

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Adverse event, non-fatal: 1
Reason: Number of subjects	Consent withdrawn by subject: 9
Reason: Number of subjects	Protocol deviation: 1
Reason: Number of subjects	Screening failure: 1
Reason: Number of subjects	Unknown: 1
Reason: Number of subjects	Missing: 1

Notes:

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

Justification: Only subjects that successfully completed the Screening period were assigned to a treatment, and randomized (enrolled). However, all subjects that underwent screening assessments signed an informed consent

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

There were no differences between DFD-29 (40mg and 20mg), Oraycea (40mg) capsules and placebo capsules in shape, size, colour or weight. The manufacturing organization was strictly independent from the sponsor's activities. No accidental unblinding by laboratory measurements was possible.

Arms

Are arms mutually exclusive?	Yes
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Arm title	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
1 capsule once daily in the morning for 16 weeks	
Arm title	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
1 capsule once daily in the morning for 16 weeks	
Arm title	Oraycea® (doxycycline) Modified Release Hard Capsules (40 mg)
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Oraycea® (doxycycline) Modified Release Hard Capsules (40 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
1 capsule once daily in the morning for 16 weeks	
Arm title	Placebo Capsules
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo Capsules
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details:	
1 capsule once daily in the morning for 16 weeks	

Number of subjects in period 1	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)	Oraycea® (doxycycline) Modified Release Hard Capsules (40 mg)
Started	53	50	49
Completed	47	38	40
Not completed	6	12	9
Consent withdrawn by subject	3	1	3
Adverse event, non-fatal	2	4	2
Subject developed and exclusion criterion	-	1	-
Unknown	-	2	1
Use of prohibited medication	-	3	2
Wrongful enrolment	-	-	-
Lost to follow-up	-	1	-
Protocol deviation	1	-	1

Number of subjects in period 1	Placebo Capsules
Started	53
Completed	35
Not completed	18
Consent withdrawn by subject	6
Adverse event, non-fatal	4
Subject developed and exclusion criterion	-
Unknown	3
Use of prohibited medication	3
Wrongful enrolment	1
Lost to follow-up	1
Protocol deviation	-

Baseline characteristics

Reporting groups

Reporting group title	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)
Reporting group description: -	
Reporting group title	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)
Reporting group description: -	
Reporting group title	Oraycea® (doxycycline) Modified Release Hard Capsules (40 m
Reporting group description: -	
Reporting group title	Placebo Capsules
Reporting group description: -	

Reporting group values	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)	Oraycea® (doxycycline) Modified Release Hard Capsules (40 m
Number of subjects	53	50	49
Age categorical Units: Subjects			
Adults (18-64 years)	45	40	40
From 65-84 years	8	10	8
From 85 and over	0	0	1
Gender categorical Units: Subjects			
Female	34	34	29
Male	19	16	20

Reporting group values	Placebo Capsules	Total	
Number of subjects	53	205	
Age categorical Units: Subjects			
Adults (18-64 years)	42	167	
From 65-84 years	11	37	
From 85 and over	0	1	
Gender categorical Units: Subjects			
Female	27	124	
Male	26	81	

Subject analysis sets

Subject analysis set title	Efficacy
Subject analysis set type	Full analysis
Subject analysis set description:	
This analysis population included all subjects who have been randomized and had at least one post baseline efficacy assessment. The FAS was the primary population for the efficacy analyses.	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

This analysis population included subjects who had at least one safety assessment post-baseline. The safety population will be employed in the analysis of tolerability and safety variables.

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

This analysis population includes all subjects who have been randomized and dispensed the study drug.

Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

This analysis population comprised all subjects who did not violate the protocol in a way that might have affected the evaluation of the effect of the study drug(s) on the primary endpoint, i.e., without major protocol violations or deviations.

Reporting group values	Efficacy	Safety	ITT
Number of subjects	200	201	205
Age categorical Units: Subjects			
Adults (18-64 years)	164	165	167
From 65-84 years	35	35	37
From 85 and over	1	1	1
Gender categorical Units: Subjects			
Female	123	123	124
Male	77	78	81

Reporting group values	Per Protocol		
Number of subjects	158		
Age categorical Units: Subjects			
Adults (18-64 years)	131		
From 65-84 years	27		
From 85 and over	0		
Gender categorical Units: Subjects			
Female	94		
Male	64		

End points

End points reporting groups

Reporting group title	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)
Reporting group description: -	
Reporting group title	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)
Reporting group description: -	
Reporting group title	Oraycea® (doxycycline) Modified Release Hard Capsules (40 m
Reporting group description: -	
Reporting group title	Placebo Capsules
Reporting group description: -	
Subject analysis set title	Efficacy
Subject analysis set type	Full analysis
Subject analysis set description:	
This analysis population included all subjects who have been randomized and had at least one post baseline efficacy assessment. The FAS was the primary population for the efficacy analyses.	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
This analysis population included subjects who had at least one safety assessment post-baseline. The safety population will be employed in the analysis of tolerability and safety variables.	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
This analysis population includes all subjects who have been randomized and dispensed the study drug.	
Subject analysis set title	Per Protocol
Subject analysis set type	Per protocol
Subject analysis set description:	
This analysis population comprised all subjects who did not violate the protocol in a way that might have affected the evaluation of the effect of the study drug(s) on the primary endpoint, i.e., without major protocol violations or deviations.	

Primary: Proportion of subjects with IGA (modified scale without erythema) 'treatment success' – Grade '0' or '1' at the end of study with at least a 2 grade reduction from Baseline to Week 16.

End point title	Proportion of subjects with IGA (modified scale without erythema) 'treatment success' – Grade '0' or '1' at the end of study with at least a 2 grade reduction from Baseline to Week 16.
End point description:	
Investigator's Global Assessment (IGA, modified scale without erythema) was carried out by visual inspection by the Investigator at every study visit from Screening up to Week 16 (or at early termination) and formed part of the clinical assessment of efficacy	
End point type	Primary
End point timeframe:	
Assessment of this endpoints were conducted at following visits: Baseline, Day 29 (+/- 5 days), Day 57 (+/- 5 days), Day 85 (+/- 5 days), Day 113 (+/- 5 days)	

End point values	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)	Oraycea® (doxycycline) Modified Release Hard Capsules (40 m	Placebo Capsules
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	47	48	52
Units: percent				
number (not applicable)	66.04	31.91	33.33	11.54

End point values	Efficacy	ITT	Per Protocol	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	200	205	158	
Units: percent				
number (not applicable)	36	38.05	41.14	

Statistical analyses

Statistical analysis title	Chi-square test
Comparison groups	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg) v DFD-29 (minocycline HCl) Extended Release Capsules (20 mg) v Oraycea® (doxycycline) Modified Release Hard Capsules (40 m v Placebo Capsules
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared

Primary: Total inflammatory lesion count (sum of papules, pustules, and nodules) reduction from Baseline to Week 16.

End point title	Total inflammatory lesion count (sum of papules, pustules, and nodules) reduction from Baseline to Week 16.
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End point description:

The total inflammatory lesion count was carried out by visual inspection by the investigator at every study visit from Screening up to Week 16 (or at early termination). Inflammatory lesions were recorded on a diagram of a human face, divided in 4 quadrants.

End point type	Primary
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End point timeframe:

Assessment of this endpoints were conducted at following visits:

Baseline, Day 29 (+/- 5 days), Day 57 (+/- 5 days), Day 85 (+/- 5 days), Day 113 (+/- 5 days)

End point values	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)	Oraycea® (doxycycline) Modified Release Hard Capsules (40 m	Placebo Capsules
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	47	48	52
Units: lesion counts				
arithmetic mean (standard deviation)	-19.2 (± 9.72)	-12.6 (± 12.92)	-10.5 (± 15.18)	-7.3 (± 10.12)

Statistical analyses

Statistical analysis title	Mixed model
Comparison groups	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg) v Oraycea® (doxycycline) Modified Release Hard Capsules (40 m v DFD-29 (minocycline HCl) Extended Release Capsules (40 mg) v Placebo Capsules
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis

Secondary: Proportion of subjects with at least a 2 grade reduction in IGA (modified scale without erythema) score from Baseline to Week 16

End point title	Proportion of subjects with at least a 2 grade reduction in IGA (modified scale without erythema) score from Baseline to Week 16
End point description:	
End point type	Secondary
End point timeframe:	
Assessment of this endpoints were conducted at following visits: Baseline, Day 29 (+/- 5 days), Day 57 (+/- 5 days), Day 85 (+/- 5 days), Day 113 (+/- 5 days)	

End point values	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)	Oraycea® (doxycycline) Modified Release Hard Capsules (40 m	Placebo Capsules
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	47	48	52
Units: percent				
number (not applicable)	69.81	36.17	37.50	17.31

End point values	Efficacy	ITT	Per Protocol	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	200	205	158	
Units: percent				
number (not applicable)	40.5	42.4	46.2	

Statistical analyses

Statistical analysis title	Chi-square test
Comparison groups	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg) v DFD-29 (minocycline HCl) Extended Release Capsules (20 mg) v Oraycea® (doxycycline) Modified Release Hard Capsules (40 m v Placebo Capsules
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared

Secondary: Median change in total RosaQoL score from Baseline to Week 16.

End point title	Median change in total RosaQoL score from Baseline to Week 16.
End point description: The RosaQoL assessment was carried out by the Investigator by asking questions as per the validated RosaQoL questionnaire instrument, at every study visit from Screening up to Week 16 (or at early termination). The subjects had to rate on a 5 grade scale their perception of the impact that rosacea had on various dimensions influencing their quality of life.	
End point type	Secondary
End point timeframe: Assessment of this endpoints were conducted at following visits: Baseline, Day 29 (+/- 5 days), Day 57 (+/- 5 days), Day 85 (+/- 5 days), Day 113 (+/- 5 days)	

End point values	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)	Oraycea® (doxycycline) Modified Release Hard Capsules (40 m	Placebo Capsules
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	47	48	52
Units: RosaQoL Score				
arithmetic mean (standard deviation)	-14.0 (± 15.58)	-9.5 (± 9.94)	-4.7 (± 10.42)	-1.7 (± 10.44)

Statistical analyses

Statistical analysis title	Kruskal-Wallis Test
Comparison groups	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg) v DFD-29 (minocycline HCl) Extended Release Capsules (20 mg) v Oraycea® (doxycycline) Modified Release Hard Capsules (40 m v Placebo Capsules
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Kruskal-wallis

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After Baseline, all new findings or worsening of a pre-existing finding (if considered clinically significant) had to be reported as Adverse event. Data pertaining to AEs were collected during each study visit.

Adverse event reporting additional description:

At each study visit, the Investigator asked a general question, e.g. "Have you experienced any other/new health problems since your last visit?" Furthermore, clinically significant findings of the physical examination, vital signs, ECG, laboratory assessments and Urinalysis were considered AEs.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)
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Reporting group description:

All patients randomized to receive DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)

Reporting group title	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)
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Reporting group description:

All Patients randomized to receive DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)

Reporting group title	Oraycea® (doxycycline) Modified Release Hard Capsules (40 mg)
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Reporting group description:

All Patients randomized to receive Oraycea® (doxycycline) Modified Release Hard Capsules (40 mg)

Reporting group title	Placebo Capsules
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Reporting group description:

All Patients randomized to receive placebo

Serious adverse events	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)	Oraycea® (doxycycline) Modified Release Hard Capsules (40 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 53 (1.89%)	2 / 48 (4.17%)	2 / 48 (4.17%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphoma			
subjects affected / exposed	0 / 53 (0.00%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papilloma			

subjects affected / exposed	0 / 53 (0.00%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	1 / 53 (1.89%)	0 / 48 (0.00%)	0 / 48 (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
Atrial fibrillation			
subjects affected / exposed	0 / 53 (0.00%)	1 / 48 (2.08%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 53 (0.00%)	1 / 48 (2.08%)	0 / 48 (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

Serious adverse events	Placebo Capsules		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphoma			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Papilloma			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery disease			

subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 52 (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: 5 %

Non-serious adverse events	DFD-29 (minocycline HCl) Extended Release Capsules (40 mg)	DFD-29 (minocycline HCl) Extended Release Capsules (20 mg)	Oraycea® (doxycycline) Modified Release Hard Capsules (40 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 53 (73.58%)	40 / 48 (83.33%)	37 / 48 (77.08%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 53 (3.77%)	1 / 48 (2.08%)	3 / 48 (6.25%)
occurrences (all)	2	2	4
Nervous system disorders			
Headache			
subjects affected / exposed	22 / 53 (41.51%)	14 / 48 (29.17%)	13 / 48 (27.08%)
occurrences (all)	47	35	37
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 53 (5.66%)	1 / 48 (2.08%)	2 / 48 (4.17%)
occurrences (all)	3	1	2
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 53 (5.66%)	1 / 48 (2.08%)	1 / 48 (2.08%)
occurrences (all)	3	1	2

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 53 (5.66%)	0 / 48 (0.00%)	1 / 48 (2.08%)
occurrences (all)	5	0	1
Abdominal pain upper			
subjects affected / exposed	2 / 53 (3.77%)	3 / 48 (6.25%)	3 / 48 (6.25%)
occurrences (all)	2	3	9
Diarrhoea			
subjects affected / exposed	4 / 53 (7.55%)	4 / 48 (8.33%)	2 / 48 (4.17%)
occurrences (all)	5	4	2
Dyspepsia			
subjects affected / exposed	2 / 53 (3.77%)	1 / 48 (2.08%)	3 / 48 (6.25%)
occurrences (all)	3	1	3
Flatulence			
subjects affected / exposed	0 / 53 (0.00%)	3 / 48 (6.25%)	0 / 48 (0.00%)
occurrences (all)	0	3	0
Nausea			
subjects affected / exposed	4 / 53 (7.55%)	2 / 48 (4.17%)	4 / 48 (8.33%)
occurrences (all)	5	2	4
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 53 (1.89%)	0 / 48 (0.00%)	3 / 48 (6.25%)
occurrences (all)	2	0	3
Pruritus			
subjects affected / exposed	0 / 53 (0.00%)	1 / 48 (2.08%)	4 / 48 (8.33%)
occurrences (all)	0	1	4
Rosacea			
subjects affected / exposed	0 / 53 (0.00%)	2 / 48 (4.17%)	2 / 48 (4.17%)
occurrences (all)	0	2	2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 53 (3.77%)	4 / 48 (8.33%)	4 / 48 (8.33%)
occurrences (all)	2	4	6
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	11 / 53 (20.75%)	8 / 48 (16.67%)	7 / 48 (14.58%)
occurrences (all)	11	11	7
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 53 (0.00%)	3 / 48 (6.25%)	0 / 48 (0.00%)
occurrences (all)	0	3	0

Non-serious adverse events	Placebo Capsules		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 52 (67.31%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 52 (25.00%)		
occurrences (all)	29		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 52 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	7		
Dyspepsia			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Flatulence</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 52 (3.85%)</p> <p>2</p> <p>0 / 52 (0.00%)</p> <p>0</p> <p>1 / 52 (1.92%)</p> <p>1</p>		
<p>Skin and subcutaneous tissue disorders</p> <p>Acne</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rosacea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>0 / 52 (0.00%)</p> <p>0</p> <p>2 / 52 (3.85%)</p> <p>2</p> <p>4 / 52 (7.69%)</p> <p>4</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 52 (11.54%)</p> <p>6</p>		
<p>Infections and infestations</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vulvovaginal mycotic infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>6 / 52 (11.54%)</p> <p>8</p> <p>0 / 52 (0.00%)</p> <p>0</p>		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 May 2017	The 4 treatment arms in the study were changed from 10 mg, 20 mg, 40 mg DFD-29 (minocycline HCL) and placebo to 20 mg and 40 mg DFD-29 (minocycline HCL), 40 mg Oraycea® (doxycycline) and placebo. In addition to the changes stated below, minor typographic errors have been corrected.
01 August 2017	The Study medication label was updated with regard to the amount contained in a bottle, contact information, storage conditions and overall information content of the label. Instead of Annex 13 to the Current Edition of the Good Manufacturing Practices Guidelines Drugs Used in Clinical Trials (GUI-0036) GCP guideline is followed.
26 February 2018	Some of the available study medication kits are expiring on July 31st 2018 and stratification of the randomization per site and IGA score resulted in a high number of kits to be stored at the individual study sites. In order to be able to use up the study medication kits with limited stability, the amount of kits on site needs to be reduced thus the stratification by IGA score is dropped.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

None reported

Notes: