Clinical trial results:
Multi-centre, Randomized, Double-blind, Placebo-Controlled Pilot Safety and Efficacy Study of 8 Weeks of Treatment with DFD-07 for Actinic Keratosis of the Face and Scalp

Summary

EudraCT number	2015-003804-21
Trial protocol	DE
Global end of trial date	27 September 2016

Results information

Result version number	v1 (current)
This version publication date	24 June 2022
First version publication date	24 June 2022

Trial information

Trial identification

Sponsor protocol code	DFD-07-CD-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Promius Pharma LLC
Sponsor organisation address	107 College Road East, Princeton, NJ, United States,
Public contact	Kent Allenby, Promius Pharma/Dr. Reddy’s Laboratories 107 College Road East Princeton, New Jersey, USA 08540, +1 609-375-9900,
Scientific contact	Flexopharm GmBH and Co. KG, Flexopharm GmBH and Co. KG, +1 609-375-9900, mail@flexopharm.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	03 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 July 2016
Global end of trial reached?	Yes
Global end of trial date	27 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary aim of the study was to investigate the efficacy of 1.25% DFD-07 after 8 weeks of self-application by the patient (1g of cream per day). The secondary aims of the study were to investigate efficacy and safety of 1.25% DFD-07 after 8 weeks of self-application by the patient and an additional follow-up period of 30 days.

Protection of trial subjects:

The incidence of treatment emergent adverse events was summarized by severity and causality in relation to the study drug for both treatment groups. The following variables were calculated for each patient for the time windows from baseline to Week 2, from Week 2 to Week 4, from Week 4 to Week 8, and from baseline to EOT and summarized by time window, treatment, center, and overall:
- Number of applications of study medication
- Percentage of required number of applications performed
- Amount (in grams) of study medication used
- Percentage of required amount of study medication used
- Mean study medication usage per application

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2015
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: 111
Worldwide total number of subjects	111
EEA total number of subjects	111

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)	0
Adults (18-64 years)	20
From 65 to 84 years	85
85 years and over	6

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Inclusion Criteria: 18 years of age and older, able to provide informed consent, skin type I, II or III according to Fitzpatrick etc.
Exclusion Criteria: Significant history of alcohol or drug abuse, pregnancy, lactation etc.

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	DFD-07

Arm description:

Patients received treatment i.e., 1.25% DFD-07 cream (30 g tube), active ingredient being Celecoxib. The cream was topically applied to the selected area by the patient, maximum use of 1g per day.

Arm type	Experimental
Investigational medicinal product name	DFD-07 cream (1.25% celecoxib cream)
Investigational medicinal product code	DFD-07
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

Twice daily application to the selected areas by the patient with maximum total use per day of 1g.

Arm title	Placebo

Arm description:

Placebo cream i.e., vehicle only (30g tube) was provided to the patients.

Arm type	Placebo
Investigational medicinal product name	Placebo Cream
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical

Dosage and administration details:

Twice daily topical application to the selected area by the patient (maximum total use 1 g per day)

Number of subjects in period 1	DFD-07	Placebo
Started	56	55
Completed	50	50
Not completed	6	5
Patient Violates Inclusion/Exclusion criteria	1	-
Missing more than 20% of product applications	-	1
Visit out of window	1	2
Missing post baseline assessment	4	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	111	111	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	20	20	
From 65-84 years	85	85	
85 years and over	6	6	
Age continuous Units: years			
arithmetic mean	72.4		
standard deviation	± 8.15	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	102	102	

End points

End points reporting groups

Reporting group title	DFD-07
Reporting group description:	
Patients received treatment i.e., 1.25% DFD-07 cream (30 g tube), active ingredient being Celecoxib. The cream was topically applied to the selected area by the patient, maximum use of 1g per day.	
Reporting group title	Placebo
Reporting group description:	
Placebo cream i.e., vehicle only (30g tube) was provided to the patients.	

Primary: Percentage of Patients with complete clearance of all AK lesions at Week 8

End point title	Percentage of Patients with complete clearance of all AK lesions at Week 8
End point description:	
End point type	Primary
End point timeframe:	
Start of the trial till Week 8	

End point values	DFD-07	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: percent				
number (not applicable)	7.7	7.8		

Statistical analyses

Statistical analysis title	Chi-Squared Test
Comparison groups	DFD-07 v Placebo
Number of subjects included in analysis	103
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9772
Method	Chi-squared

Secondary: Percent of patients with complete clearance of AK lesions at the End of Study (EOS) Visit (8 weeks treatment plus 30-day follow up)

End point title	Percent of patients with complete clearance of AK lesions at the End of Study (EOS) Visit (8 weeks treatment plus 30-day follow up)

End point description:

End point type	Secondary

End point timeframe:

Start of the trial to End of Study (8 weeks+ 30 days follow up)

End point values	DFD-07	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: percent				
number (not applicable)	20	10		

Statistical analyses

Statistical analysis title	Chi-Squared Test
Comparison groups	DFD-07 v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1614
Method	Chi-squared

Secondary: Percentage of patients with complete clearance of AK lesions at Week 4

End point title	Percentage of patients with complete clearance of AK lesions at Week 4

End point description:

End point type	Secondary

End point timeframe:

Start of the trial till week 4

End point values	DFD-07	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	53		
Units: percent				
number (not applicable)	1.9	1.9		

Statistical analyses

Statistical analysis title	Chi-Squared Test
Comparison groups	DFD-07 v Placebo
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Chi-squared

Secondary: Percentage of patients with partial clearance of AK lesions at Weeks 4 and 8 and EOS Visit

End point title	Percentage of patients with partial clearance of AK lesions at Weeks 4 and 8 and EOS Visit

End point description:

End point type	Secondary

End point timeframe:

Partial clearance is defined as at least a 75% reduction in the number of AK lesions in the treatment area compared to Baseline. Analysis is performed at week 4, week 8 and end of study.

End point values	DFD-07	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: percent				
number (not applicable)	36	18		

Statistical analyses

Statistical analysis title	Chi-Squared Test
Comparison groups	DFD-07 v Placebo
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0426
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for reporting adverse event was at visit 2, visit 3, visit 4 (end of treatment) and visit 5 (end of study)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	DFD-07
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	DFD-07	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 56 (0.00%)	0 / 55 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	DFD-07	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 56 (25.00%)	25 / 55 (45.45%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Lymphoma			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Squamous cell carcinoma of head and neck			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	

Viral acanthoma			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Spinal compression fracture			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Skin abrasion			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Cardiovascular disorder			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Dermabrasion			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Nervous system disorders			
Burning sensation			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	1 / 56 (1.79%)	2 / 55 (3.64%)	
occurrences (all)	1	2	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	1 / 56 (1.79%)	2 / 55 (3.64%)	
occurrences (all)	1	2	
Deafness unilateral			

subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Hypoacusis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Eye inflammation			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Drug eruption			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 56 (1.79%)	2 / 55 (3.64%)	
occurrences (all)	1	2	
Pain of skin			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	2 / 56 (3.57%)	0 / 55 (0.00%)	
occurrences (all)	2	0	
Rosacea			

subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	
occurrences (all)	1	1	
Skin lesion			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Skin ulcer			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Asteatosis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Skin mass			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 56 (1.79%)	1 / 55 (1.82%)	
occurrences (all)	1	1	
Synovial cyst			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Erysipeloid			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Flea infestation			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Herpes simplex			

subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	3 / 56 (5.36%)	7 / 55 (12.73%)	
occurrences (all)	3	7	
Gastrointestinal fungal infection			
subjects affected / exposed	0 / 56 (0.00%)	1 / 55 (1.82%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	1 / 56 (1.79%)	0 / 55 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 56 (0.00%)	2 / 55 (3.64%)	
occurrences (all)	0	2	

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