Clinical trial results:
Double-blind, randomised clinical study comparing efficacy and safety of Clindamycin/Benzoyl Peroxide Gel (10 mg/g + 50 mg/g) (Test) vs. DUAC Akne Gel (Reference) vs. Vehicle in patients with papulopustular acne

Summary

EudraCT number	2017-000522-36
Trial protocol	DE
Global end of trial date	02 June 2021

Results information

Result version number	v1 (current)
This version publication date	18 April 2022
First version publication date	18 April 2022

Trial information

Trial identification

Sponsor protocol code	17-02/ClinBPO-50

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dermapharm AG
Sponsor organisation address	Lil-Dagover-Ring 7, Gruenwald, Germany, 82031
Public contact	Clinical Research Department, Dermapharm AG, +49 89641860, Clinicaltrials.Dermapharm@dermapharm.com
Scientific contact	Clinical Research Department, Dermapharm AG, +49 89641860, Clinicaltrials.Dermapharm@dermapharm.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 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 June 2021
Global end of trial reached?	Yes
Global end of trial date	02 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the efficacy and safety of a new gel containing 10 mg/g Clindamycin and 50 mg/g Benzoyl peroxide vs. DUAC Akne Gel (Reference) vs. vehicle in patients with papulopustular acne

Protection of trial subjects:

In the current clinical trial patients below the age of 18 have been included. In such a case, an age-appropriate written subject information sheet was handed over to adolescent patients and an appropriate information session was to be performed by the investigator. The legal guardian(s) received a comparable document and an information session for adults. Before the start of screening and randomisation for the current clinical trial, the legal guardian(s) had to sign the informed consent form(s) and the adolescent patient the informed assent form. In case any of the parties (legal guardian(s) or adolescent patient) refused their consent, a participation of the adolescent patient in the trial was not possible.

Background therapy:

There was no background therapy.

Evidence for comparator:

The comparator contains the same ingredients in the same concentration as the test product and has a marketing license for the study indication.

Actual start date of recruitment	22 August 2018
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: 674
Worldwide total number of subjects	674
EEA total number of subjects	674

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)	282
Adults (18-64 years)	392
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

18 study centers in Germany; first patient first visit: 17 September 2018; last patient last visit: 02 June 2021

Pre-assignment

Screening details:

Main criteria for inclusion: Women, men and adolescents of ≥ 12 years of age; Diagnosis of "papulopustular acne" according to generally accepted criteria; On the face, ≥ 25 non-inflammatory lesions and ≥ 20 inflammatory lesions, thereof ≤ 2 nodular lesions; Investigator`s Global Assessment (IGA) of acne severity grade 2, 3 or 4

Period 1

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

Blinding implementation details:

The tubes containing the study medications were neutral white. The attached labels were identical for all three preparations. All three study medications were indistinguishable with respect to visual or odorous characteristics. The random code was transferred to the data base not before the following actions were completed: data base closure, finalisation of the statistical analysis plan, a Blind Data Review and a subsequent Blind Data Report.

Arms

Are arms mutually exclusive?	Yes
Arm title	ClinBPO 50

Arm description:

Test product

Arm type	Experimental
Investigational medicinal product name	Clindamycin/Benzoyl Peroxide Gel (10 mg/g + 50 mg/g)
Investigational medicinal product code	D10AF51
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

The study medication had to be applied to the washed treatment area, i.e. acne affected area on the face, once daily in the evening. The gel should be applied in such a thin film that the gel rubs easily into the skin. Face was considered as the area bounded by ears, hairline and lower margin of the mandibles. Contact with mouth, eyes, lips, other mucous membranes, or areas of irritated or broken skin should be avoided.

Arm title	DUAC Akne

Arm description:

Reference Product

Arm type	Active comparator
Investigational medicinal product name	DUAC Akne Gel
Investigational medicinal product code	D10AF51
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

The study medication had to be applied to the washed treatment area, i.e. acne affected area on the

face, once daily in the evening. The gel should be applied in such a thin film that the gel rubs easily into the skin. Face was considered as the area bounded by ears, hairline and lower margin of the mandibles. Contact with mouth, eyes, lips, other mucous membranes, or areas of irritated or broken skin should be avoided.

Arm title	Vehicle
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	D10AF51
Other name	
Pharmaceutical forms	Gel
Routes of administration	Cutaneous use

Dosage and administration details:

The study medication had to be applied to the washed treatment area, i.e. acne affected area on the face, once daily in the evening. The gel should be applied in such a thin film that the gel rubs easily into the skin. Face was considered as the area bounded by ears, hairline and lower margin of the mandibles. Contact with mouth, eyes, lips, other mucous membranes, or areas of irritated or broken skin should be avoided.

Number of subjects in period 1	ClinBPO 50	DUAC Akne	Vehicle
Started	223	224	227
Completed	208	203	195
Not completed	15	21	32
Consent withdrawn by subject	4	3	1
Adverse event, non-fatal	1	4	3
Poor compliance	1	2	3
COVID-19 related	1	-	-
Lost to follow-up	4	9	6
Lack of efficacy	4	3	19

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period

Reporting group description: -

Reporting group values	Treatment Period	Total	
Number of subjects	674	674	
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)	282	282	
Adults (18-64 years)	392	392	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	442	442	
Male	232	232	

Subject analysis sets	
Subject analysis set title	Safety data set
Subject analysis set type	Safety analysis

Subject analysis set description:

Comprises all randomised patients who had administered the study medication at least once and who provided at least one safety related outcome.

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

Consists of all patients as randomised who received study medication at least once and have a baseline assessment and at least one post-baseline assessment of the number of papulopustular acne lesions.

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

Comprises all patients of the FAS who do not exhibit any major protocol violations.

Reporting group values	Safety data set	FAS	PP
Number of subjects	674	672	597
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0

Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	282	281	262
Adults (18-64 years)	392	391	335
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	442	441	381
Male	232	231	216

End points

End points reporting groups

Reporting group title	ClinBPO 50
Reporting group description: Test product	
Reporting group title	DUAC Akne
Reporting group description: Reference Product	
Reporting group title	Vehicle
Reporting group description: -	
Subject analysis set title	Safety data set
Subject analysis set type	Safety analysis
Subject analysis set description: Comprises all randomised patients who had administered the study medication at least once and who provided at least one safety related outcome.	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description: Consists of all patients as randomised who received study medication at least once and have a baseline assessment and at least one post-baseline assessment of the number of papulopustular acne lesions.	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description: Comprises all patients of the FAS who do not exhibit any major protocol violations.	

Primary: Treatment effect (inflammatory lesions)

End point title	Treatment effect (inflammatory lesions)
End point description:	
End point type	Primary
End point timeframe: Treatment start (Visit 1) to end-of-treatment (EOT) examination at Visit V8 (week 12).	

End point values	ClinBPO 50	DUAC Akne	Vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	199	195	227	
Units: percent change				
arithmetic mean (standard deviation)	84.6 (± 22.43)	81.8 (± 25.42)	50.7 (± 41.61)	

Statistical analyses

Statistical analysis title	Analysis of efficacy
Statistical analysis description: The first part of the primary objective of this study was to show therapeutic equivalence of the test preparation ClinBPO 50 as compared to the reference DUAC Akne. Therapeutic equivalence was	

statistically proven if the two-sided 95% confidence interval (CI) for μ INFL-ClinBPO 50 - μ INFL-DUAC Akne was completely contained within [-10.0, 10.0].

Comparison groups	ClinBPO 50 v DUAC Akne
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (final values)
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.95
upper limit	7.54

Statistical analysis title	Superiority of Test over Vehicle

Statistical analysis description:

In order to verify assay sensitivity of the study design, superiority of the two active preparations over vehicle was tested by means of two-sided significance tests with α = 0.05. The primary test of superiority was carried out for the FAS data set.

Comparison groups	ClinBPO 50 v Vehicle
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Statistical analysis title	Superiority of Reference over Vehicle

Statistical analysis description:

In order to verify assay sensitivity of the study design, superiority of the two active preparations over vehicle was tested by means of two-sided significance tests with α = 0.05. The primary test of superiority was carried out for the FAS data set.

Comparison groups	DUAC Akne v Vehicle
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Primary: Treatment effect (total number of lesions)

End point title	Treatment effect (total number of lesions)

End point description:

End point type	Primary

End point timeframe:

s. Timeframe "Treatment effect (inflammatory lesions)"

End point values	ClinBPO 50	DUAC Akne	Vehicle	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	199	195	227	
Units: percent change				
arithmetic mean (standard deviation)	80.2 (± 22.64)	77.3 (± 24.30)	49.1 (± 35.03)	

Statistical analyses

Statistical analysis title	Analysis of efficacy

Statistical analysis description:

The first part of the primary objective of this study was to show therapeutic equivalence of the test preparation ClinBPO 50 as compared to the reference DUAC Akne. Therapeutic equivalence was statistically proven if the two-sided 95% confidence interval (CI) for μ TOTAL-ClinBPO 50 - μ TOTAL-DUAC Akne was completely contained within [-10.0, 10.0].

Comparison groups	ClinBPO 50 v DUAC Akne
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	Mean difference (final values)
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.79
upper limit	7.51

Statistical analysis title	Superiority of Test over Vehicle

Statistical analysis description:

In order to verify assay sensitivity of the study design, superiority of the two active preparations over vehicle was tested by means of two-sided significance tests with α = 0.05. The primary test of superiority was carried out for the FAS data set.

Comparison groups	ClinBPO 50 v Vehicle
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Statistical analysis title	Superiority of Reference over Vehicle

Statistical analysis description:

In order to verify assay sensitivity of the study design, superiority of the two active preparations over vehicle was tested by means of two-sided significance tests with α = 0.05. The primary test of

superiority was carried out for the FAS data set.

Comparison groups	DUAC Akne v Vehicle
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From inclusion visit (day 0, Visit V1) to end-of-treatment (EOT) examination at Visit V8 (week 12).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	ClinBPO 50
Reporting group description: Test product	
Reporting group title	DUAC Akne
Reporting group description: Reference Product	
Reporting group title	Vehicle
Reporting group description: -	

Serious adverse events	ClinBPO 50	DUAC Akne	Vehicle
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 222 (0.45%)	1 / 224 (0.45%)	1 / 228 (0.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (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
Ear and labyrinth disorders			
Vestibular disorder			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			

subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	ClinBPO 50	DUAC Akne	Vehicle
Total subjects affected by non-serious adverse events			
subjects affected / exposed	108 / 222 (48.65%)	111 / 224 (49.55%)	79 / 228 (34.65%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibrous histiocytoma			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Skin papilloma			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Dental operation			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Limb operation			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Wisdom teeth removal			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Application site dryness			
subjects affected / exposed	16 / 222 (7.21%)	16 / 224 (7.14%)	12 / 228 (5.26%)
occurrences (all)	16	16	12
Application site erythema			
subjects affected / exposed	7 / 222 (3.15%)	5 / 224 (2.23%)	1 / 228 (0.44%)
occurrences (all)	7	6	1
Application site exfoliation			

subjects affected / exposed	5 / 222 (2.25%)	3 / 224 (1.34%)	0 / 228 (0.00%)
occurrences (all)	5	3	0
Application site irritation			
subjects affected / exposed	0 / 222 (0.00%)	3 / 224 (1.34%)	0 / 228 (0.00%)
occurrences (all)	0	3	0
Application site pain			
subjects affected / exposed	3 / 222 (1.35%)	4 / 224 (1.79%)	1 / 228 (0.44%)
occurrences (all)	4	4	1
Application site pruritus			
subjects affected / exposed	2 / 222 (0.90%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	2	1	0
Application site reaction			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Application site swelling			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Inflammation			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	3 / 222 (1.35%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	3	1	0
Immune system disorders			
Allergy to metals			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Atopy			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Drug hypersensitivity			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1

Food allergy			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Hypersensitivity			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 222 (0.90%)	4 / 224 (1.79%)	0 / 228 (0.00%)
occurrences (all)	3	4	0
Oropharyngeal pain			
subjects affected / exposed	2 / 222 (0.90%)	1 / 224 (0.45%)	3 / 228 (1.32%)
occurrences (all)	2	1	3
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Investigations			
Arthroscopy			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Vitamin D decreased			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	2 / 222 (0.90%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	2	0	0
Foreign body in eye			

subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Hand fracture			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Ligament rupture			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Product administered at inappropriate site			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Scar			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
Dermoid cyst			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Nervous system disorders			
Burning sensation			
subjects affected / exposed	16 / 222 (7.21%)	22 / 224 (9.82%)	6 / 228 (2.63%)
occurrences (all)	19	24	6
Headache			

subjects affected / exposed	12 / 222 (5.41%)	3 / 224 (1.34%)	11 / 228 (4.82%)
occurrences (all)	13	4	13
Migraine			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Motion sickness			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Eye disorders			
Eye swelling			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Swelling of eyelid			
subjects affected / exposed	0 / 222 (0.00%)	2 / 224 (0.89%)	0 / 228 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 222 (0.45%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	2	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	1 / 228 (0.44%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	3 / 222 (1.35%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	3	0	0
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	2 / 222 (0.90%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	2	0	0
Toothache			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	5 / 228 (2.19%)
occurrences (all)	0	1	5
Alopecia areata			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Dermal cyst			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	2 / 228 (0.88%)
occurrences (all)	0	0	2
Dry skin			
subjects affected / exposed	14 / 222 (6.31%)	21 / 224 (9.38%)	2 / 228 (0.88%)
occurrences (all)	16	23	3
Dyshidrotic eczema			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	2	0	0
Eczema			
subjects affected / exposed	1 / 222 (0.45%)	1 / 224 (0.45%)	1 / 228 (0.44%)
occurrences (all)	1	1	1
Eczema asteatotic			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	15 / 222 (6.76%)	18 / 224 (8.04%)	5 / 228 (2.19%)
occurrences (all)	16	18	5

Hand dermatitis			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	1	0	1
Keloid scar			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Mechanical urticaria			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Papule			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	9 / 222 (4.05%)	14 / 224 (6.25%)	2 / 228 (0.88%)
occurrences (all)	11	14	2
Rash			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Skin burning sensation			
subjects affected / exposed	1 / 222 (0.45%)	2 / 224 (0.89%)	1 / 228 (0.44%)
occurrences (all)	1	2	1
Skin exfoliation			
subjects affected / exposed	8 / 222 (3.60%)	12 / 224 (5.36%)	5 / 228 (2.19%)
occurrences (all)	8	14	5
Skin irritation			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Skin tightness			
subjects affected / exposed	2 / 222 (0.90%)	5 / 224 (2.23%)	3 / 228 (1.32%)
occurrences (all)	2	5	3
Solar dermatitis			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	1 / 228 (0.44%)
occurrences (all)	0	1	1

Renal and urinary disorders			
Urinary tract pain			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 222 (0.00%)	2 / 224 (0.89%)	1 / 228 (0.44%)
occurrences (all)	0	2	1
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Acarodermatitis			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	2	0	1
Bronchitis			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	0 / 222 (0.00%)	2 / 224 (0.89%)	0 / 228 (0.00%)
occurrences (all)	0	2	0
Conjunctivitis			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	1 / 228 (0.44%)
occurrences (all)	0	1	1
Cystitis			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Cystitis bacterial			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Fungal skin infection			

subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	2 / 222 (0.90%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	2	1	0
Gastrointestinal infection			
subjects affected / exposed	2 / 222 (0.90%)	1 / 224 (0.45%)	1 / 228 (0.44%)
occurrences (all)	2	1	1
Herpes simplex			
subjects affected / exposed	1 / 222 (0.45%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	1	1	0
Hordeolum			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	1	0	1
Infection			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Infectious mononucleosis			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	23 / 222 (10.36%)	25 / 224 (11.16%)	15 / 228 (6.58%)
occurrences (all)	25	30	16
Oral herpes			
subjects affected / exposed	1 / 222 (0.45%)	1 / 224 (0.45%)	2 / 228 (0.88%)
occurrences (all)	1	1	2
Otitis media			
subjects affected / exposed	2 / 222 (0.90%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	2	0	0
Paronychia			

subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	1 / 222 (0.45%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	1	1	0
Pyelitis			
subjects affected / exposed	1 / 222 (0.45%)	0 / 224 (0.00%)	0 / 228 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 222 (0.45%)	1 / 224 (0.45%)	1 / 228 (0.44%)
occurrences (all)	1	1	1
Rhinitis			
subjects affected / exposed	2 / 222 (0.90%)	2 / 224 (0.89%)	0 / 228 (0.00%)
occurrences (all)	2	2	0
Tinea pedis			
subjects affected / exposed	0 / 222 (0.00%)	0 / 224 (0.00%)	1 / 228 (0.44%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	2 / 222 (0.90%)	2 / 224 (0.89%)	0 / 228 (0.00%)
occurrences (all)	2	3	0
Urinary tract infection			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Arthralgia			
subjects affected / exposed	0 / 222 (0.00%)	1 / 224 (0.45%)	0 / 228 (0.00%)
occurrences (all)	0	1	0

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

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

None reported

Notes: