Clinical trial results:
A Randomised, Double-Blind, Vehicle-Controlled Phase 2 Study of Topically Applied INM-755 (cannabinol) Cream in Patients with Epidermolysis Bullosa.

Summary

EudraCT number	2021-000214-42
Trial protocol	DE FR AT GR IT ES
Global end of trial date	19 April 2023

Results information

Result version number	v1 (current)
This version publication date	13 April 2024
First version publication date	13 April 2024

Trial information

Trial identification

Sponsor protocol code	755-201-EB

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04908215
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	InMed Pharmaceuticals Inc.
Sponsor organisation address	Suite 310 - 815 West Hastings Street, Vancouver, Canada, V6C 1B4
Public contact	Clinical Research Executive, InMed Pharmaceuticals Inc., 1 604-669-7207, clinical@inmedpharma.com
Scientific contact	Clinical Research Executive, InMed Pharmaceuticals Inc., 1 604-669-7207, clinical@inmedpharma.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	19 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 April 2023
Global end of trial reached?	Yes
Global end of trial date	19 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the safety of INM-755 cream in patients with EB.
- To obtain preliminary evidence of efficacy of INM-755 cream on wound and non-wound affected skin areas in patients with EB.

Protection of trial subjects:

No special measures were required for this Phase 2 study of a topical cream product. If an important adverse reaction to the cream were to occur, it would simply be washed off and/or not re-applied in accordance with normal investigator oversight and patient preference.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	France: 5
Worldwide total number of subjects	19
EEA total number of subjects	17

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)	3

Adults (18-64 years)	15
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment of patients for this very rare disease was undertaken in 6 EU countries (Austria, France, Germany, Greece, Italy, and Spain) and Israel. No patients were enrolled in Austria or Spain. The first patient was screened on 15Dec2021 in Israel and enrolled (first treatment) on 28Dec2021. The last patient was enrolled 10Mar2023.

Pre-assignment

Screening details:

Overall 27 subjects were screened: 4 subjects were screen failures immediately, 4 were SFs at the end of baseline observation week. A total of 19 patients were enrolled and received INM-755 cream and Vehicle cream. This study used a within-patient randomisation of pairs of matched index areas (1 area to INM-755 therapy and 1 area to Vehicle cream).

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, Carer, Assessor

Blinding implementation details:

Each patient could have a matched pair of non-wound index areas, wound index areas, or both. Each index area in a matched pair was randomised to INM-755 cream or Vehicle cream in a 1:1 ratio in a blinded manner. Study creams were identical in appearance and labelled in a blinded way. No study site personnel, patient, Sponsor personnel, or Sponsor designee who was involved in study conduct decisions was unblinded to treatment assignment throughout the duration of the study.

Arms

Are arms mutually exclusive?	No
Arm title	Non-Wound INM-755

Arm description:

Non-wound index area within a matched pair assigned to INM-755 treatment

Arm type	Experimental
Investigational medicinal product name	INM-755 (cannabinol) Cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use, Topical

Dosage and administration details:

For non-wound index areas, the application of the study drug (either INM-755 cream or Vehicle cream) was done once daily, applied by the patient or caregiver directly on the index area skin in a typical thin layer (approximately 2 mg cream per cm2 of skin) and gently rubbed into the skin. Patients were given practical instructions on how to measure a suitable amount of cream using Fingertip Units calculated for the size of the area being treated. No dressing was required, but it was optional per the patient's preference. Treatment was to be given for a maximum of 28 days (Days 1 to 28).

Arm title	Non-Wound Vehicle

Arm description:

Non-wound index area within a matched pair assigned to Vehicle control treatment

Arm type	vehicle control

Investigational medicinal product name	Vehicle Cream
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Cutaneous use, Topical

Dosage and administration details:

For non-wound index areas, the application of the study drug (either INM-755 cream or Vehicle cream) was done once daily, applied by the patient or caregiver directly on the index area skin in a typical thin layer (approximately 2 mg cream per cm2 of skin) and gently rubbed into the skin. Patients were given practical instructions on how to measure a suitable amount of cream using Fingertip Units calculated for the size of the area being treated. No dressing was required, but it was optional per the patient's preference. Treatment was to be given for a maximum of 28 days (Days 1 to 28).

Number of subjects in period 1	Non-Wound INM-755	Non-Wound Vehicle
Started	18	18
Week 1	18	18
Week 2	18	18
Week 3	18	18
Week 4	17	17
Completed	17	17
Not completed	1	1
Adverse event, non-fatal	1	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period

Reporting group description:

19 patients were enrolled and treated. Each patient had at least one pair of matched index areas treated with INM-755 and Vehicle in a randomized blinded manner. 17 patients had 1 pair of matched non-wound (NW) Index areas. 1 patient had 1 pair of matched wound (W) Index areas. 1 patient had both 1 pair of NW index areas and 1 pair of W index areas. N=18 patients for NW index areas, N=2 for W index areas.

Reporting group values	Treatment Period	Total	
Number of subjects	19	19	
Age categorical Units: Subjects			
Adolescents (12-17 years)	3	3	
Adults (18-64 years)	15	15	
From 65-84 years	1	1	
Age continuous Units: years			
arithmetic mean	35.3		
standard deviation	± 15.39	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	8	8	
Race Units: Subjects			
White	19	19	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	16	16	
Unknown/Not Reported	3	3	
Fitzpatrick Skin Type			
Skin Type scale based on skin colour and sensitivity to sun			
Units: Subjects			
Fitzpatrick Skin Type I	2	2	
Fitzpatrick Skin Type II	6	6	
Fitzpatrick Skin Type III	10	10	
Fitzpatrick Skin Type IV	1	1	
Fitzpatrick Skin Type V	0	0	
Fitzpatrick Skin Type VI	0	0	
Epidermolysis bullosa (EB) Type			
Genetic subtype of epidermolysis bullosa			
Units: Subjects			
EB Simplex	4	4	
EB Junctional	2	2	
EB Dominant Dystrophic	2	2	
EB Recessive Dystrophic	9	9	

EB Kindler	2	2	

Subject analysis sets

Subject analysis set title	Safety Analysis Set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SAF consisted of all index areas (non-wound or wound) that received INM-755 cream or matching Vehicle cream. The SAF was used for safety summaries and analysis of local effects. All patients who received the study drug were assessed for systemic effects.
A total of 19 patients were enrolled and treated; 18 patients had non-wound index pairs and 2 patients had wound index pairs. One of the 19 patients had both non-wound and wound index pairs. Within each index pair, one skin area was randomized to INM-755 and one was randomized to Vehicle, in a blinded manner.

Subject analysis set title	Pharmacokinetic Analysis Set (PKS)
Subject analysis set type	Safety analysis

Subject analysis set description:

The PKS included all patients who received at least one dose of the study drug and had at least one PK concentration measured.
Provision of a single blood sample at the end of treatment for measurement of plasma cannabinol concentration was optional and 14 patients consented for that procedure.

Subject analysis set title	Non-wound Itch Evaluable Analysis Set (ESA)
Subject analysis set type	Per protocol

Subject analysis set description:

All non-wound index areas meeting the eligibility criterion of non-wound itch ≥40 mm on Visual Analogue Scale (VAS, 0-100 mm) during the Baseline Observation Period (1 week before randomization and treatment initiation).

*If a randomisation error was detected after database lock (once unblinding had occurred) then the SAF analysis set was to be used, in order to consider the effect of the actual treatment. This is what was done. It was an analysis "as treated".

Reporting group values	Safety Analysis Set (SAF)	Pharmacokinetic Analysis Set (PKS)	Non-wound Itch Evaluable Analysis Set (ESA)
Number of subjects	19	14	14
Age categorical Units: Subjects			
Adolescents (12-17 years)	3	0	2
Adults (18-64 years)	15	13	11
From 65-84 years	1	1	1
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female	11	6	9
Male	8	8	5
Race Units: Subjects			
White	19	14	14
Ethnicity			

Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	16	11	13
Unknown/Not Reported	3	3	1
Fitzpatrick Skin Type			
Skin Type scale based on skin colour and sensitivity to sun			
Units: Subjects			
Fitzpatrick Skin Type I	2	1	2
Fitzpatrick Skin Type II	6	5	3
Fitzpatrick Skin Type III	10	7	8
Fitzpatrick Skin Type IV	1	1	1
Fitzpatrick Skin Type V	0	0	0
Fitzpatrick Skin Type VI	0	0	0
Epidermolysis bullosa (EB) Type			
Genetic subtype of epidermolysis bullosa			
Units: Subjects			
EB Simplex	4	2	3
EB Junctional	2	2	0
EB Dominant Dystrophic	2	2	2
EB Recessive Dystrophic	9	6	7
EB Kindler	2	2	2

End points

End points reporting groups

Reporting group title	Non-Wound INM-755

Reporting group description:

Non-wound index area within a matched pair assigned to INM-755 treatment

Reporting group title	Non-Wound Vehicle

Reporting group description:

Non-wound index area within a matched pair assigned to Vehicle control treatment

Subject analysis set title	Safety Analysis Set (SAF)
Subject analysis set type	Safety analysis

Subject analysis set description:

The SAF consisted of all index areas (non-wound or wound) that received INM-755 cream or matching Vehicle cream. The SAF was used for safety summaries and analysis of local effects. All patients who received the study drug were assessed for systemic effects.
A total of 19 patients were enrolled and treated; 18 patients had non-wound index pairs and 2 patients had wound index pairs. One of the 19 patients had both non-wound and wound index pairs. Within each index pair, one skin area was randomized to INM-755 and one was randomized to Vehicle, in a blinded manner.

Subject analysis set title	Pharmacokinetic Analysis Set (PKS)
Subject analysis set type	Safety analysis

Subject analysis set description:

The PKS included all patients who received at least one dose of the study drug and had at least one PK concentration measured.
Provision of a single blood sample at the end of treatment for measurement of plasma cannabinol concentration was optional and 14 patients consented for that procedure.

Subject analysis set title	Non-wound Itch Evaluable Analysis Set (ESA)
Subject analysis set type	Per protocol

Subject analysis set description:

All non-wound index areas meeting the eligibility criterion of non-wound itch ≥40 mm on Visual Analogue Scale (VAS, 0-100 mm) during the Baseline Observation Period (1 week before randomization and treatment initiation).

*If a randomisation error was detected after database lock (once unblinding had occurred) then the SAF analysis set was to be used, in order to consider the effect of the actual treatment. This is what was done. It was an analysis "as treated".

Primary: NW Itch: Within-patient difference in CFB (INM-755 - Vehicle)

End point title	NW Itch: Within-patient difference in CFB (INM-755 - Vehicle)

End point description:

Patients scored itch once daily for each non-wound (NW) index area within a matched pair (one area received INM-755, the other received Vehicle, as randomized and blinded). Itch was scored on the Visual Analogue Scale (0-100 mm), with 0 score meaning no itch and 100 score meaning the worst imaginable itch. Average weekly Itch scores were calculated for each index area and within-patient comparisons of INM-755 and Vehicle were tested using paired t-tests of the Change from Baseline (CFB). Note for interpretation: A negative value for within-patient difference in CFB (INM-755 - Vehicle) would favour INM-755.

End point type	Primary

End point timeframe:

Weekly for 4 weeks

End point values	Non-Wound INM-755	Non-Wound Vehicle	Non-wound Itch Evaluable Analysis Set (ESA)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	14[1]	14[2]	14[3]	
Units: mm				
arithmetic mean (standard deviation)				
Week 1	-19.224 (± 27.2640)	-17.786 (± 18.9561)	-1.439 (± 15.8467)	
Week 2	-19.306 (± 27.3566)	-20.194 (± 24.9994)	0.888 (± 7.6389)	
Week 3	-23.19 (± 23.9680)	-23.614 (± 24.8766)	0.424 (± 15.6356)	
Week 4	-32.021 (± 26.6676)	-29.867 (± 26.8017)	-2.155 (± 14.3983)	

Notes:

[1] - NW index areas excluded from ESA for 4 pts; 1 patient missing Week 4

[2] - NW index areas excluded from ESA for 4 pts; 1 patient missing Week 4

[3] - The within-patient difference in CFB for matched index areas (INM-755 - Vehicle). 1 missing Wk 4.

Statistical analyses

Statistical analysis title	NW Itch: Within-patient Paired t-test, Week 4

Statistical analysis description:

Average weekly Itch scores were calculated for each index area and within-patient comparisons of INM-755 and Vehicle were tested using paired t-tests of the Change from Baseline (CFB). A negative value for within-patient difference in CFB (INM-755 - Vehicle) favours INM-755.

Comparison groups	Non-Wound INM-755 v Non-Wound Vehicle
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5994 [4]
Method	paired t-test
Parameter estimate	Mean difference (final values)
Point estimate	-2.155
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.8554
upper limit	6.5462
Variability estimate	Standard deviation
Dispersion value	14.3983

Notes:

[4] - p-values at earlier timepoints:
Week 1 = 0.7395
Week 2 = 0.6708
Week 3 = 0.9206

Secondary: PIC-I: Within-patient difference in CFB (INM-755 - Vehicle)

End point title	PIC-I: Within-patient difference in CFB (INM-755 - Vehicle)

End point description:

PIC-I = Patient's Impression of Change for Non-wound Itch. This was reported by the patient after 2 and 4 weeks of treatment for each of the matched index areas (one treated with INM-755, one with Vehicle). They scored their impression of change from baseline, using the Dynamic Pruritus Scale (+50 mm for maximal improvement (almost no itch remaining) to -50 mm (maximal worsening of itch), with 0 mm for no change. Note for interpretation: A positive result for within patient difference (PIC-I INM-755

minus PIC-I Vehicle) would indicate a better outcome on itch for INM-755 compared with Vehicle on the basis of PIC-I.

End point type	Secondary

End point timeframe:

Week 2 and Week 4

End point values	Non-Wound INM-755	Non-Wound Vehicle	Non-wound Itch Evaluable Analysis Set (ESA)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	14[5]	14[6]	14[7]	
Units: mm				
arithmetic mean (standard deviation)				
Week 2	9.7 (± 24.85)	12.6 (± 29.22)	-2.9 (± 12.64)	
Week 4	10.0 (± 28.00)	7.5 (± 31.68)	2.5 (± 14.07)	

Notes:

[5] - 4 pts excluded from ESA. Missing data for 1 pt at Week 2 (n=13). At Week 4 n=14.

[6] - 4 pts excluded from ESA. Missing data for 1 pt at Week 2 (n=13). At Week 4 n=14.

[7] - Missing data for 1 pt at Week 2 (n=13). At Week 4 n=14.

Statistical analyses

Statistical analysis title	PIC-I CFB: Within-patient Paired t-test, Week 4
Comparison groups	Non-Wound INM-755 v Non-Wound Vehicle
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5178 [8]
Method	paired t-test
Parameter estimate	Mean difference (final values)
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.62
upper limit	10.62
Variability estimate	Standard deviation
Dispersion value	14.07

Notes:

[8] - p-value at Week 2 = 0.4206

Other pre-specified: Plasma Cannabinol Concentration, End of Study

End point title	Plasma Cannabinol Concentration, End of Study

End point description:

It was optional for patients to provide a single blood sample for analysis at the end of treatment. 14 patients consented to this. Most samples were drawn within 0-2 days after last dose. For 3 patients, the samples were at 5, 7, and 19 days after last dose. Limit of quantitation was 1.0 pg/mL.

End point type	Other pre-specified

End point timeframe:
Week 4 (End of Study)

End point values	Pharmacokinetic Analysis Set (PKS)			
Subject group type	Subject analysis set			
Number of subjects analysed	14			
Units: pg/mL				
median (full range (min-max))	4.850 (0.00 to 176.00)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire treatment period: From first dose of study treatment until completion of therapy (max 4 weeks), and 1 week additional safety follow-up.

Adverse event reporting additional description:

AEs were collected at weekly visits and recorded as local or systemic.
Local AEs in index areas: treatment-emergent (TE) local AEs were summarised by treatment, severity, association with treatment or dressings.
Other Local AEs (in untreated areas).
Systemic AEs: TE systemic AEs were summarised by severity, association with treatment

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	INM-755 Treated Non-wound Index Areas, Local AEs

Reporting group description:

This is the group of NW Index Areas treated with INM-755. Each patient with matched pairs of NW Index Areas received both treatments, one area treated with INM-755, the other with Vehicle (randomised, blinded).

Reporting group title	INM-755 Treated Wound Index Areas, Local AEs

Reporting group description:

This is the group of Wound Index Areas treated with INM-755. Each patient with matched pairs of Wound Index Areas received both treatments, one area treated with INM-755, the other with Vehicle (randomised, blinded).

Reporting group title	Vehicle Treated Non-wound Index Areas, Local AEs

Reporting group description:

This is the group of NW Index Areas treated with Vehicle. Each patient with matched pairs of NW Index Areas received both treatments, one area treated with INM-755, the other with Vehicle (randomised, blinded).

Reporting group title	Vehicle Treated Wound Index Areas, Local AEs

Reporting group description:

This is the group of Wound Index Areas treated with Vehicle. Each patient with matched pairs of Wound Index Areas received both treatments, one area treated with INM-755, the other with Vehicle (randomised, blinded).

Reporting group title	Untreated Areas, Local AEs

Reporting group description:

AEs were categorized as local or systemic. These local areas were not treated. The underlying disease (epidermolysis bullosa) is characterized by many skin lesions.

Reporting group title	All Treated Patients, Systemic AEs

Reporting group description:

All patients received both INM-755 and Vehicle as topical treatments on matched index area pairs. These are the systemic AEs reported, not the AEs that occurred locally at the treated index areas or in other local untreated areas.

Serious adverse events	INM-755 Treated Non-wound Index Areas, Local AEs	INM-755 Treated Wound Index Areas, Local AEs	Vehicle Treated Non-wound Index Areas, Local AEs
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Endocarditis	Additional description: Endocarditis after 3 weeks of treatment, assessed as not related to masked study treatment. In the opinion of the Investigator, the event was due to the underlying medical condition of cardiomyopathy. Hospitalised, study treatment interrupted.		
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Vehicle Treated Wound Index Areas, Local AEs	Untreated Areas, Local AEs	All Treated Patients, Systemic AEs
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Endocarditis	Additional description: Endocarditis after 3 weeks of treatment, assessed as not related to masked study treatment. In the opinion of the Investigator, the event was due to the underlying medical condition of cardiomyopathy. Hospitalised, study treatment interrupted.		
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
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: 5 %

Non-serious adverse events	INM-755 Treated Non-wound Index Areas, Local AEs	INM-755 Treated Wound Index Areas, Local AEs	Vehicle Treated Non-wound Index Areas, Local AEs
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 18 (16.67%)	0 / 2 (0.00%)	2 / 18 (11.11%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	1 / 18 (5.56%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Eczema asteatotic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 2 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Erythema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 2 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	2 / 18 (11.11%)	0 / 2 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1
Pseudofolliculitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Endocarditis			

subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 2 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Vehicle Treated Wound Index Areas, Local AEs	Untreated Areas, Local AEs	All Treated Patients, Systemic AEs
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	3 / 19 (15.79%)	7 / 19 (36.84%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	4
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Blister			
subjects affected / exposed	0 / 2 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0

Eczema asteatotic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pseudofolliculitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			
subjects affected / exposed	0 / 2 (0.00%)	1 / 19 (5.26%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Endocarditis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 19 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

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