Clinical trial results:
A randomized, double-blind, multi-centre, placebo-controlled, parallel-arm phase 2 trial to assess safety, efficacy and pharmacokinetics of CD11301 0.03% and 0.06% gel in the treatment of Cutaneous T-Cell Lymphoma (CTCL), stages IA, IB and IIA

Summary

EudraCT number	2017-001677-16
Trial protocol	DE FR
Global end of trial date	17 March 2020

Results information

Result version number	v1 (current)
This version publication date	28 March 2021
First version publication date	28 March 2021

Trial information

Trial identification

Sponsor protocol code	RD.03.SPR.104003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03292406
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Galderma R&D SNC
Sponsor organisation address	Les Templiers, 2400 route des Colles, Biot, France, 06410
Public contact	CTA Coordinator, Galderma R&D SNC, +33 493-95-70-85, cta.coordinator@galderma.com
Scientific contact	CTA Coordinator, Galderma R&D SNC, +33 493-95-70-85, cta.coordinator@galderma.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	17 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy and safety of two concentrations (0.03% and 0.06%) of CD11301 gel in the treatment of CTCL (stage IA, IB, or IIA) versus placebo.

Protection of trial subjects:

This clinical trial was conducted in accordance with the protocol, the Helsinki declaration (1964) and subsequent amendments, and the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP), and in compliance with applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 December 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 48
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Germany: 29
Worldwide total number of subjects	86
EEA total number of subjects	38

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)	45
From 65 to 84 years	41
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 3 countries (France, Germany, USA) between 19 Dec 2017 to 17 Mar 2020. A total of 86 subjects were randomized to 1 of the 3 treatment groups (placebo gel or CD11301 gel 0.03% or 0.06%) in a 1:1:1 ratio.

Pre-assignment

Screening details:

This study consisted of 2 cycles: Cycle 1 and Cycle 2. Each treatment cycle consisted of 8 weeks on treatment followed by 4 weeks without treatment. Cycle 1: drug product was applied on up to 5 percent (%) body surface area (BSA) and 10% BSA in cycle 2.

Period 1

Period 1 title	Overall Period (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	CD11301 Gel 0.06%

Arm description:

Subjects applied 0.06% CD11301 gel (up to 500 mg per dose) topically once daily, 3 to 5 times per week, for cycle 1 and 2 i.e. 24 weeks.

Arm type	Experimental
Investigational medicinal product name	CD11301 gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Subjects applied (either 0.03% or 0.06%) of CD11301 gel topically for 24 weeks.

Arm title	CD11301 Gel 0.03%

Arm description:

Subjects applied 0.03% CD11301 gel (up to 500 mg per dose) topically once daily, 3 to 5 times per week, for cycle 1 and 2 i.e. 24 weeks.

Arm type	Experimental
Investigational medicinal product name	CD11301 gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Subjects applied (either 0.03% or 0.06%) of CD11301 gel topically for 24 weeks.

Arm title	Placebo

Arm description:

Subjects applied placebo gel during cycle one followed by 0.03% CD11301 gel topically during cycle two once daily, 3 to 5 times per week, for 24 weeks.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Subjects applied placebo gel during cycle one for 24 weeks.

Investigational medicinal product name	CD11301 gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Subjects applied (0.03% and 0.06%) of CD11301 gel topically for 24 weeks.

Number of subjects in period 1	CD11301 Gel 0.06%	CD11301 Gel 0.03%	Placebo
Started	30	28	28
Subjects Treated	30	28	27
Completed	17	15	15
Not completed	13	13	13
Consent withdrawn by subject	-	7	2
Adverse event, non-fatal	7	1	4
Progressive Disease	6	3	4
Unspecified	-	1	2
Protocol deviation	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	CD11301 Gel 0.06%
Reporting group description:	
Subjects applied 0.06% CD11301 gel (up to 500 mg per dose) topically once daily, 3 to 5 times per week, for cycle 1 and 2 i.e. 24 weeks.	
Reporting group title	CD11301 Gel 0.03%
Reporting group description:	
Subjects applied 0.03% CD11301 gel (up to 500 mg per dose) topically once daily, 3 to 5 times per week, for cycle 1 and 2 i.e. 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects applied placebo gel during cycle one followed by 0.03% CD11301 gel topically during cycle two once daily, 3 to 5 times per week, for 24 weeks.	

Reporting group values	CD11301 Gel 0.06%	CD11301 Gel 0.03%	Placebo
Number of subjects	30	28	28
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)	0	0	0
Adults (18-64 years)	15	17	13
From 65-84 years	15	11	15
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	8	8	12
Male	22	20	16

Reporting group values	Total		
Number of subjects	86		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	45		
From 65-84 years	41		
85 years and over	0		

Gender categorical Units: Subjects			
Female	28		
Male	58		

End points

End points reporting groups

Reporting group title	CD11301 Gel 0.06%
Reporting group description:	
Subjects applied 0.06% CD11301 gel (up to 500 mg per dose) topically once daily, 3 to 5 times per week, for cycle 1 and 2 i.e. 24 weeks.	
Reporting group title	CD11301 Gel 0.03%
Reporting group description:	
Subjects applied 0.03% CD11301 gel (up to 500 mg per dose) topically once daily, 3 to 5 times per week, for cycle 1 and 2 i.e. 24 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects applied placebo gel during cycle one followed by 0.03% CD11301 gel topically during cycle two once daily, 3 to 5 times per week, for 24 weeks.	

Primary: Number of Subjects Reported Overall Response (OR) (Complete and Partial [CR or PR]) of Target Treated Lesions Based on Modified Composite Assessment of Index Lesion Severity (mCAILS) Score at Week 12

End point title	Number of Subjects Reported Overall Response (OR) (Complete and Partial [CR or PR]) of Target Treated Lesions Based on Modified Composite Assessment of Index Lesion Severity (mCAILS) Score at Week 12
End point description:	
OR is defined as the number of subjects that achieved a CR or PR as assessed by mCAILS. mCAILS total was derived from components collected on the case report form (CRF).Target treated lesions(1-5 lesions) were rated in erythema (0-8, where 0=no evidence and 8=very severe), scaling(0-8,where 0=no evidence and 8=very severe), plaque elevation (0-3,where 0=no evidence and 3=marked elevation), and size (scale=0-18, where 0=no measurable area and 18=size of lesion >300 centimeter [cm]^2). These 4 ratings were summed to create subtotals, 1 per lesion.Final mCAILS assessment score was the sum of these subtotals.Total summation Score: 0-50 where higher score indicated higher severity. CR is defined as a 100% decrease from baseline i.e. score of '0' on the mCAILS scale. PR is defined as at least a 50%, but less than 100%, decrease from baseline. ITT Population included all randomized subjects. Here, overall number of subjects analyzed signifies subjects who were evaluable for this endpoint.	
End point type	Primary
End point timeframe:	
Week 12	

End point values	CD11301 Gel 0.06%	CD11301 Gel 0.03%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	7	1	
Units: Subjects				
Complete Response	0	2	0	
Partial Response	4	5	1	

Statistical analyses

Statistical analysis title	Placebo versus CD11301 0.06%
Statistical analysis description:	
Difference in Response Rate from Placebo (SE)	
Comparison groups	CD11301 Gel 0.06% v Placebo
Number of subjects included in analysis	5
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3446
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted Difference in Response R
Point estimate	10.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.2
upper limit	26.6

Statistical analysis title	Placebo versus CD11301 0.03%
Comparison groups	CD11301 Gel 0.03% v Placebo
Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.1088
Method	Cochran-Mantel-Haenszel
Parameter estimate	Strata-adjusted Difference in Response R
Point estimate	20
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-4.5
upper limit	41.1

Notes:

[1] - Strata-adjusted Difference in Response Rate from Placebo was analyzed and reported.

Secondary: Number of Subjects Reported Overall Response (OR) of Target Treated Lesions Based on Modified Severity- Weighted Assessment Tool (mSWAT) Score at Week 12

End point title	Number of Subjects Reported Overall Response (OR) of Target Treated Lesions Based on Modified Severity- Weighted Assessment Tool (mSWAT) Score at Week 12

End point description:

OR is defined as the number of subjects that achieved a CR or PR as assessed by mSWAT. mSWAT composite score involved the direct assessment of the BSA of each type of lesion (palm plus fingers of the subject= approximately 1% BSA) in each of 12 areas (Head, Neck, Anterior trunk, Arms, Forearms, Hands, Posterior trunk, Buttocks, Thighs, Legs, Feet, Groin) of the body, multiplying the sum of the BSA of each lesion type by a weighting factor (patch = 1, plaque = 2, and tumor = 3 or 4) and generating a sum of the subtotals of each lesion subtype. mSWAT score (0=no lesions; 400= lesions covering all areas). CR is defined as a 100% decrease from baseline. PR is defined as at least a 50%, but less than 100%, decrease from baseline, and with a tumor subscore of zero (no tumor). ITT Population included all randomized subjects. Here, overall number of subjects analyzed signifies number of subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	CD11301 Gel 0.06%	CD11301 Gel 0.03%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	4	2	
Units: subjects				
Complete Response	0	0	0	
Partial Response	6	4	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Subject's First Overall Response (Complete or Partial) of the Target Treated Lesions Based on the mCAILS Score

End point title	Time to Subject's First Overall Response (Complete or Partial) of the Target Treated Lesions Based on the mCAILS Score

End point description:

Time to OR (CR or PR) is the number of days from the start of drug application to the first documentation of OR assessed by mCAILS Score. The 25th, 50th, and 75th percentiles were presented along with 95% confidence intervals using the log-log transformation. ITT Population included all randomized subjects. Here, overall number of subjects analyzed signifies subjects who were evaluable for this endpoint. Here 99999 indicates Missing quartiles and CIs were non-estimable due to a lack of events.

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	CD11301 Gel 0.06%	CD11301 Gel 0.03%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	12	1	
Units: Days				
number (confidence interval 95%)				
25th (95% CI)	169 (84 to 169.0)	85 (83 to 174)	99999 (85.0 to 99999)	
50th (95% CI)	197 (169 to 257)	99999 (99999 to 99999)	99999 (99999 to 99999)	
75th (95% CI)	257 (197 to 257)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Overall Response (Complete Response or Partial Response) Based on mCAILS Score

End point title	Duration of Overall Response (Complete Response or Partial Response) Based on mCAILS Score

End point description:

The duration of OR (CR or PR) of the target treated lesions based on the mCAILS score was calculated in days as: (date of first non-response after responding) – (date of response) + 1. mCAILS assessment total was derived from components collected on CRF. Target treated lesions (1-5 lesions) were rated in erythema (0-8, where 0=no evidence and 8=very severe), scaling (0-8, where 0=no evidence and 8=very severe), plaque elevation (0-3, where 0=no evidence and 3=marked elevation), and size (scale=0-18, where 0=no measurable area and 18= size of lesion >300 cm^2). These 4 ratings were summed to create subtotals, 1 per lesion. Final mCAILS assessment score was sum of these subtotals. Total summation Score: 0-50 where higher score indicated higher severity. ITT Population included all randomized subjects. Here, overall number of subjects analyzed signifies subjects who were evaluable for this endpoint. Here 99999 indicates missing quartiles and CIs were non-estimable due to lack of events.

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	CD11301 Gel 0.06%	CD11301 Gel 0.03%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	10	1	
Units: Days				
number (confidence interval 95%)				
25th (95% CI)	133 (29.0 to 141.0)	99999 (38.0 to 99999)	99999 (99999 to 99999)	
50th (95% CI)	141 (133.0 to 99999)	99999 (38.0 to 99999)	99999 (99999 to 99999)	
75th (95% CI)	99999 (133.0 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progressive Disease Using mSWAT

End point title	Time to Progressive Disease Using mSWAT

End point description:

Progressive disease is defined as ≥ 25% increase in skin disease from baseline, or loss of response: in those with CR or PR, increase of skin score of greater than the sum of nadir plus 50% baseline score, Nadir is defined as the lowest skin score (best response). ITT Population included all randomized subjects. Here, overall number of subjects analyzed signifies number of subjects who were evaluable for this endpoint. Here 99999 and -99999 indicates missing quartiles and CIs were non-estimable due to a lack of events.

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	CD11301 Gel 0.06%	CD11301 Gel 0.03%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	21	24	
Units: Days				
number (confidence interval 95%)				
25th (95% CI)	99999 (170 to 99999)	191 (85 to 99999)	93 (85 to 93)	
50th (95% CI)	99999 (99999 to 99999)	99999 (99999 to 99999)	93 (-99999 to 99999)	
75th (95% CI)	99999 (99999 to 99999)	99999 (99999 to 99999)	93 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Skindex-29 Survey Results at Week 12, 24 and 36

End point title	Change From Baseline in Skindex-29 Survey Results at Week 12, 24 and 36

End point description:

Subjects answered 30 questions as part of the Skindex-29 survey. A composite score and 3 sub scores were calculated from the results. Item 18 of the survey was not used in any scoring. First, answers to each item were given a numeric value: Never = 0; Rarely = 25; Sometimes = 50; Often = 75; All the time = 100. The items used to calculate each subscore were: Emotions: 3, 6, 9, 12, 13, 15, 21, 23, 26, and 28 (10 items), Symptoms: 1, 7, 10, 16, 19, 24, and 27 (7 items), Functioning: 2, 4, 5, 8, 11, 14, 17, 20, 22, 25, 29, and 30 (12 items). The composite score is the average of the 3 sub scores ranging from 0 (no effect)-100 (maximum effect), higher score corresponds to lower quality of life. ITT Population included all randomized subjects. Here, overall number of subjects analyzed signifies subjects who were evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Week 12, 24 and Follow up (Week 36)

End point values	CD11301 Gel 0.06%	CD11301 Gel 0.03%	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	28	27	
Units: score on scale				
arithmetic mean (standard deviation)				
Week 12	1.93 (± 12.408)	-0.27 (± 8.583)	-1.58 (± 13.243)	
Week 24 (n=23, 26, 24)	-2.16 (± 11.651)	-3.36 (± 9.816)	0.58 (± 16.059)	

Week 36 (n= 22, 19, 20)	-3.30 (± 14.838)	-3.22 (± 8.340)	-0.34 (± 14.081)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of the study drug administration up to end of the study (Week 72)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
Subjects applied 0.06% CD11301 gel (up to 500 mg per dose) topically once daily, 3 to 5 times per week, for 24 weeks.	
Reporting group title	Group 2
Reporting group description:	
Subjects applied 0.03% CD11301 gel (up to 500 mg per dose) topically once daily, 3 to 5 times per week, for 24 weeks.	
Reporting group title	Group 3
Reporting group description:	
Subjects applied placebo gel during cycle one followed by 0.03% CD11301 gel topically during cycle two once daily, 3 to 5 times per week, for 24 weeks.	

Serious adverse events	Group 1	Group 2	Group 3
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 30 (6.67%)	2 / 28 (7.14%)	1 / 27 (3.70%)
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)			
Lung adenocarcinoma			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metastases to bone			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metastases to central nervous system			

subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metastases to muscle			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Papillary cystadenoma lymphomatosum			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	0 / 27 (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
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	0 / 27 (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
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
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	Group 1	Group 2	Group 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)	28 / 28 (100.00%)	27 / 27 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Mycosis fungoides			
subjects affected / exposed	3 / 30 (10.00%)	4 / 28 (14.29%)	5 / 27 (18.52%)
occurrences (all)	3	4	5
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 30 (10.00%)	2 / 28 (7.14%)	1 / 27 (3.70%)
occurrences (all)	3	2	1
General disorders and administration site conditions			
Application site dermatitis			
subjects affected / exposed	4 / 30 (13.33%)	3 / 28 (10.71%)	1 / 27 (3.70%)
occurrences (all)	4	3	1
Application site eczema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Application site erosion			
subjects affected / exposed	9 / 30 (30.00%)	3 / 28 (10.71%)	2 / 27 (7.41%)
occurrences (all)	9	3	2
Application site erythema			
subjects affected / exposed	7 / 30 (23.33%)	5 / 28 (17.86%)	2 / 27 (7.41%)
occurrences (all)	7	5	2
Application site inflammation			
subjects affected / exposed	0 / 30 (0.00%)	6 / 28 (21.43%)	1 / 27 (3.70%)
occurrences (all)	0	6	1
Application site irritation			
subjects affected / exposed	1 / 30 (3.33%)	5 / 28 (17.86%)	1 / 27 (3.70%)
occurrences (all)	1	5	1
Application site pain			
subjects affected / exposed	6 / 30 (20.00%)	3 / 28 (10.71%)	2 / 27 (7.41%)
occurrences (all)	6	3	2
Application site pruritus			
subjects affected / exposed	4 / 30 (13.33%)	8 / 28 (28.57%)	4 / 27 (14.81%)
occurrences (all)	4	8	4
Application site rash			
subjects affected / exposed	2 / 30 (6.67%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	2	1	0
Application site ulcer			

subjects affected / exposed	8 / 30 (26.67%)	8 / 28 (28.57%)	2 / 27 (7.41%)
occurrences (all)	8	8	2
Asthenia			
subjects affected / exposed	1 / 30 (3.33%)	2 / 28 (7.14%)	0 / 27 (0.00%)
occurrences (all)	1	2	0
Chills			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	3 / 27 (11.11%)
occurrences (all)	1	0	3
Fatigue			
subjects affected / exposed	5 / 30 (16.67%)	5 / 28 (17.86%)	2 / 27 (7.41%)
occurrences (all)	5	5	2
Influenza like illness			
subjects affected / exposed	6 / 30 (20.00%)	3 / 28 (10.71%)	2 / 27 (7.41%)
occurrences (all)	6	3	2
Pyrexia			
subjects affected / exposed	3 / 30 (10.00%)	2 / 28 (7.14%)	0 / 27 (0.00%)
occurrences (all)	3	2	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 30 (6.67%)	2 / 28 (7.14%)	0 / 27 (0.00%)
occurrences (all)	2	2	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 30 (13.33%)	1 / 28 (3.57%)	1 / 27 (3.70%)
occurrences (all)	4	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 30 (6.67%)	1 / 28 (3.57%)	1 / 27 (3.70%)
occurrences (all)	2	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 30 (6.67%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	2	1	0

Urine leukocyte esterase positive			
subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	2
White blood cell count decreased			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 30 (0.00%)	1 / 28 (3.57%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
Bundle branch block left			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 30 (23.33%)	5 / 28 (17.86%)	1 / 27 (3.70%)
occurrences (all)	7	5	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 30 (13.33%)	1 / 28 (3.57%)	0 / 27 (0.00%)
occurrences (all)	4	1	0
Nausea			
subjects affected / exposed	4 / 30 (13.33%)	2 / 28 (7.14%)	2 / 27 (7.41%)
occurrences (all)	4	2	2
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 30 (0.00%)	2 / 28 (7.14%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Dry skin			

subjects affected / exposed	1 / 30 (3.33%)	0 / 28 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	2
Erythema			
subjects affected / exposed	1 / 30 (3.33%)	1 / 28 (3.57%)	2 / 27 (7.41%)
occurrences (all)	1	1	2
Night sweats			
subjects affected / exposed	0 / 30 (0.00%)	2 / 28 (7.14%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Papule			
subjects affected / exposed	1 / 30 (3.33%)	2 / 28 (7.14%)	0 / 27 (0.00%)
occurrences (all)	1	2	0
Pruritus			
subjects affected / exposed	2 / 30 (6.67%)	3 / 28 (10.71%)	5 / 27 (18.52%)
occurrences (all)	2	3	5
Rash			
subjects affected / exposed	0 / 30 (0.00%)	2 / 28 (7.14%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Rash maculo-papular			
subjects affected / exposed	0 / 30 (0.00%)	0 / 28 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Skin erosion			
subjects affected / exposed	5 / 30 (16.67%)	2 / 28 (7.14%)	1 / 27 (3.70%)
occurrences (all)	5	2	1
Skin ulcer			
subjects affected / exposed	0 / 30 (0.00%)	2 / 28 (7.14%)	2 / 27 (7.41%)
occurrences (all)	0	2	2
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 30 (3.33%)	1 / 28 (3.57%)	2 / 27 (7.41%)
occurrences (all)	1	1	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
Back pain			

subjects affected / exposed	4 / 30 (13.33%)	1 / 28 (3.57%)	1 / 27 (3.70%)
occurrences (all)	4	1	1
Myalgia			
subjects affected / exposed	2 / 30 (6.67%)	1 / 28 (3.57%)	1 / 27 (3.70%)
occurrences (all)	2	1	1
Infections and infestations			
Folliculitis			
subjects affected / exposed	1 / 30 (3.33%)	3 / 28 (10.71%)	0 / 27 (0.00%)
occurrences (all)	1	3	0
Fungal skin infection			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Hordeolum			
subjects affected / exposed	2 / 30 (6.67%)	0 / 28 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 30 (10.00%)	3 / 28 (10.71%)	2 / 27 (7.41%)
occurrences (all)	3	3	2
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 30 (13.33%)	4 / 28 (14.29%)	0 / 27 (0.00%)
occurrences (all)	4	4	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 30 (6.67%)	1 / 28 (3.57%)	1 / 27 (3.70%)
occurrences (all)	2	1	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 February 2018	Amendment 1: Updated the CAILS assessment tool to modified CAILS, on the recommendation of industry investigator experts. -Clarified total daily dosage of investigational product throughout the protocol. -Clarified how the dosing amount to be applied on each subject was determined. -Clarified why women of childbearing potential were allowed in the study. -Clarified why women of childbearing potential were allowed in the study. -Added responsibility of the IDMC. -Added recruitment procedures to the protocol. -Allowed subjects to be re-screened once. -Allowed documentation of histological finding of CTCL within last 12 months or to perform a skin biopsy to confirm during the screening visit if one was not available. -Expanded the B0 definition for inclusion criteria #4. - Updated the double-barrier contraception method. - Changed the wording about the systemic pharmacodynamics assessment. -All centers were asked to collect blood samples for immune cell dynamics. -Removed all proteomic biomarker assessments.
16 April 2018	Amendment 2: Inclusion criterion was added: BfArM requested that subjects only be permitted to participate in the trial after the German S2K guidelines for cutaneous lymphoma treatment were either contraindicated, insufficiently effective, or poorly tolerated.
25 March 2019	Amendment 3: - Amended withdrawal criteria in case of disease progression such that an assessment of progressive disease in subjects with stage IA MF-CTCL at Baseline presenting a -25% increase in skin disease (mSWAT) would not be clinically meaningful if the BSA affected were <10%. - Change of sponsor address and phone number. - Extended the study to follow complete responders of mSWAT at Week 36 up to Week 72 or until relapse. - Clarification of inclusion criterion #4: subjects were required to be B0. - Addendum to the clinical study report to provide time to relapse. - Clarification of pregnancy tests.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported