Clinical trial results:
A multicenter open label uncontrolled study of the long term safety and efficacy of calcitriol 3 mcg/g ointment applied twice daily for 26 weeks in pediatric subjects (2 to 16 years and 11 months of age) with mild to moderate plaque psoriasis

Summary

EudraCT number	2014-000710-53
Trial protocol	DE IT BE HU
Global end of trial date	29 May 2018

Results information

Result version number	v1 (current)
This version publication date	25 September 2020
First version publication date	25 September 2020

Trial information

Trial identification

Sponsor protocol code	RD.06.SPR.18131

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02125279
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 (0)493-95-70-85, cta.coordinator@galderma.com
Scientific contact	CTA Coordinator, GALDERMA R&D, SNC, +33 (0)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	28 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 May 2018
Global end of trial reached?	Yes
Global end of trial date	29 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of up to 26 weeks of treatment with calcitriol 3 mcg/g ointment when used twice daily, without occlusion, to treat pediatric subjects (2 to 16 years and 11 months of age) with plaque psoriasis.

Protection of trial subjects:

This study was performed in compliance with Good Clinical Practice (GCP) including the archiving of essential study documents. All data provided either to the Investigator (and study staff) or collected during the study and/or reported herein should be regarded as confidential and proprietary in nature and should not be disclosed to any third party without the written consent of Galderma.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 May 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	United States: 32
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 5
Worldwide total number of subjects	54
EEA total number of subjects	11

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	34
Adolescents (12-17 years)	20
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The original intent of the study was to screen approximately 167 subjects in order to enroll a target of 100 subjects. However due to slow study enrollment and in agreement with the Food and Drug Administration, the study was closed to enrollment in November 2017.

Pre-assignment

Screening details:

A total of 88 subjects were screened. Only 54 subjects out of 88 were enrolled and received study drug, of which 41 subjects completed the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Calcitriol 3 mcg/g

Arm description:

Subjects received calcitriol 3 microgram per gram (mcg/g) ointment applied twice daily without exceeding a maximum of 0.5 gram per kilogram (g/kg) of body weight or 28 gram (g) daily (whichever was the lower) up to 26 weeks. Subjects were further followed up for 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Calcitriol
Investigational medicinal product code	
Other name	CD2027
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

Subjects applied calcitriol 3 microgram per gram (mcg/g) ointment applied twice daily up to 26 weeks

Number of subjects in period 1	Calcitriol 3 mcg/g
Started	54
Completed	41
Not completed	13
Consent withdrawn by subject	6
Lost to follow-up	4
Lack of efficacy	2
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
All enrolled subjects who have applied the study drug at least once during the study.	

Reporting group values	Overall Study	Total	
Number of subjects	54	54	
Age categorical Units: Subjects			
Children (2-11 years)	34	34	
Adolescents (12-17 years)	20	20	
Age continuous Units: years			
arithmetic mean	10.3		
standard deviation	± 3.99	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	30	30	
Race (NIH/OMB) Units: Subjects			
Asian	4	4	
Black or African American	1	1	
White	46	46	
Unknown or Not Reported	3	3	

End points

End points reporting groups

Reporting group title	Calcitriol 3 mcg/g

Reporting group description:

Subjects received calcitriol 3 microgram per gram (mcg/g) ointment applied twice daily without exceeding a maximum of 0.5 gram per kilogram (g/kg) of body weight or 28 gram (g) daily (whichever was the lower) up to 26 weeks. Subjects were further followed up for 4 weeks.

Primary: Change From Screening in Serum Albumin Levels at Week 4

End point title	Change From Screening in Serum Albumin Levels at Week 4[1]

End point description:

Change from screening (the last test prior to the first study medication application) in serum albumin levels at week 4 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening and Week 4

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	48[2]			
Units: gram per liter (g/L)				
arithmetic mean (standard deviation)	-1.0 (± 2.28)			

Notes:

[2] - Number of evaluable subjects for this endpoint

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Albumin Levels at Week 8

End point title	Change From Screening in Serum Albumin Levels at Week 8[3]

End point description:

Change from screening (the last test prior to the first study medication application) in serum albumin levels at week 8 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 8

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: g/L				
arithmetic mean (standard deviation)	-1.0 (± 2.09)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Albumin Levels at Week 12

End point title	Change From Screening in Serum Albumin Levels at Week 12[4]

End point description:

Change from screening (the last test prior to the first study medication application) in serum albumin levels at week 12 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 12

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: g/L				
arithmetic mean (standard deviation)	-0.8 (± 2.03)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Albumin Levels at Week 20

End point title	Change From Screening in Serum Albumin Levels at Week 20[5]

End point description:

Change from screening (the last test prior to the first study medication application) in serum albumin levels at week 20 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 20

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: g/L				
arithmetic mean (standard deviation)	-1.1 (± 2.10)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Albumin Levels at Week 26

End point title	Change From Screening in Serum Albumin Levels at Week 26[6]

End point description:

Change from screening (the last test prior to the first study medication application) in serum albumin levels at week 26 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 26

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: g/L				
arithmetic mean (standard deviation)	-0.8 (± 2.09)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Albumin Levels at Week 30 (Follow-up)

End point title	Change From Screening in Serum Albumin Levels at Week 30 (Follow-up)[7]

End point description:

Change from screening (the last test prior to the first study medication application) in serum albumin levels at week 30 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 30 (Follow-up)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: g/L				
arithmetic mean (standard deviation)	-0.2 (± 2.95)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Urine Calcium/Creatinine Ratio at Week 12

End point title	Change From Screening in Urine Calcium/Creatinine Ratio at Week 12[8]

End point description:

Change from screening (the last test prior to the first study medication application) in urine calcium/creatinine ratio at week 12 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 12

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Ratio				
arithmetic mean (standard deviation)	-0.0164 (± 0.14340)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Urine Calcium/Creatinine Ratio at Week 26

End point title	Change From Screening in Urine Calcium/Creatinine Ratio at Week 26[9]

End point description:

Change from screening (the last test prior to the first study medication application) in urine calcium/creatinine ratio at week 26 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 26

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Ratio				
arithmetic mean (standard deviation)	0.0456 (± 0.15588)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Urine Calcium/Creatinine Ratio at Week 30 (Follow-up)

End point title	Change From Screening in Urine Calcium/Creatinine Ratio at Week 30 (Follow-up)[10]

End point description:

Change from screening (the last test prior to the first study medication application) in urine calcium/creatinine ratio at week 30 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 30 (Follow-up)

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Ratio				
arithmetic mean (standard deviation)	0.0715 (± 0.14333)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Phosphate Levels at Week 4

End point title	Change From Screening in Serum Phosphate Levels at Week

End point description:

Change from screening (the last test prior to the first study medication application) in serum phosphate levels at week 4 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 4

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: mmol/L				
arithmetic mean (standard deviation)	0.0334 (± 0.17093)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Phosphate Levels at Week 12

End point title	Change From Screening in Serum Phosphate Levels at Week

End point description:

Change from screening (the last test prior to the first study medication application) in serum phosphate levels at week 12 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 12

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: mmol/L				
arithmetic mean (standard deviation)	0.0237 (± 0.17996)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Phosphate Levels at Week 20

End point title	Change From Screening in Serum Phosphate Levels at Week

End point description:

Change from screening (the last test prior to the first study medication application) in serum phosphate levels at week 20 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 20

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: mmol/L				
arithmetic mean (standard deviation)	0.0079 (± 0.19925)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Phosphate Levels at Week 26

End point title	Change From Screening in Serum Phosphate Levels at Week

End point description:

Change from screening (the last test prior to the first study medication application) in serum phosphate levels at week 26 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 26

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: mmol/L				
arithmetic mean (standard deviation)	0.0091 (± 0.21262)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Phosphate Levels at Week 30 (Follow-up)

End point title	Change From Screening in Serum Phosphate Levels at Week 30 (Follow-up)[15]

End point description:

Change from screening (the last test prior to the first study medication application) in serum phosphate levels at week 30 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 30 (Follow-up)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: mmol/L				
arithmetic mean (standard deviation)	0.0145 (± 0.18727)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 4

End point title	Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 4[16]

End point description:

Change from screening (the last test prior to the first study medication application) in serum PTH levels at week 4 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 4

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: pmol/L				
arithmetic mean (standard deviation)	0.14 (± 0.967)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 8

End point title	Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 8[17]

End point description:

Change from screening (the last test prior to the first study medication application) in serum PTH levels at week 8 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 8

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: pmol/L				
arithmetic mean (standard deviation)	0.09 (± 1.451)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 12

End point title	Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 12[18]

End point description:

Change from screening (the last test prior to the first study medication application) in serum PTH levels at week 12 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 12

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: pmol/L				
arithmetic mean (standard deviation)	0.04 (± 1.400)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 20

End point title	Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 20[19]

End point description:

Change from screening (the last test prior to the first study medication application) in serum PTH levels at week 20 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 20

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: pmol/L				
arithmetic mean (standard deviation)	0.17 (± 1.152)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 26

End point title	Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 26[20]

End point description:

Change from screening (the last test prior to the first study medication application) in serum PTH levels at week 26 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 26

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: pmol/L				
arithmetic mean (standard deviation)	-0.07 (± 1.744)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 30 (Follow-up)

End point title	Change From Screening in Serum Parathyroid Hormone (PTH) Levels at Week 30 (Follow-up)[21]

End point description:

Change from screening (the last test prior to the first study medication application) in serum PTH levels at week 30 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 30 (Follow-up)

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: pmol/L				
arithmetic mean (standard deviation)	0.37 (± 1.796)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)[22]

End point description:

An adverse event (AE) is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory value), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. A TEAE is defined as an AE with an onset date on or after the first application of the study drug. Safety population included as all the subjects who have applied the study drug at least once.

End point type	Primary

End point timeframe:

Up to Week 30

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: Number of subjects	20			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Screening in Serum Phosphate Levels at Week 8

End point title	Change From Screening in Serum Phosphate Levels at Week

End point description:

Change from screening (the last test prior to the first study medication application) in serum phosphate levels at week 8 were reported. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable for this outcome measure.

End point type	Primary

End point timeframe:

Screening, Week 8

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No inferential statistical analysis was planned and performed for this endpoint.

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: mmol/L				
arithmetic mean (standard deviation)	-0.0137 (± 0.15541)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Investigator’s Global Assessment of Disease Severity (IGA) Score of 0 (Clear) or 1 (Almost Clear) at Each Visit

End point title	Number of Subjects With Investigator’s Global Assessment of Disease Severity (IGA) Score of 0 (Clear) or 1 (Almost Clear) at Each Visit

End point description:

The IGA is a 0 to 4 point scale. Where, 0 = clear (no signs of psoriasis except for residual hypopigmentation/hyperpigmentation); 1 = almost clear (just perceptible erythema, no induration, and no scaling); 2 = mild (mild erythema, no induration, and mild or no scaling); 3 = moderate (moderate erythema, mild induration, and mild or no scaling); 4 = severe (severe erythema, moderate to severe induration, and scaling of any degree). Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable this outcome measure and 'n' (number of subjects analyzed) signifies number of subjects evaluable for each time point.

End point type	Secondary

End point timeframe:

Weeks 4, 8, 12, 20, 26 and 30 (Follow-up)

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Number of subjects				
Week 4 (n=51)	3			
Week 8 (n=32)	5			
Week 12 (n=49)	15			
Week 20 (n=29)	14			
Week 26 (n=41)	19			
Week 30 (n=41)	17			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pruritus Score at Each Visit

End point title	Change From Baseline in Pruritus Score at Each Visit

End point description:

Pruritus was scored on a 0 to 4 point scale. Where, 0 = none (no-itching); 1 = mild (slight itching, not really bothersome); 2 = moderate (definite itching that is somewhat bothersome without loss of sleep); 3 = severe (intense itching that has caused pronounced discomfort, night rest interrupted); 4 = very severe (very severe itching that has caused pronounced discomfort during the night and daily activities). Positive change from baseline indicate worsening of indication. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' (overall number of subjects analyzed) signifies number of subjects evaluable this outcome measure and 'n' (number of subjects analyzed) signifies number of subjects evaluable for each time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 20, 26 and 30 (Follow-up)

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 4 (n=51)	-0.6 (± 0.85)			
Week 8 (n=32)	-0.7 (± 0.64)			
Week 12 (n=49)	-0.7 (± 0.88)			
Week 20 (n=29)	-0.7 (± 0.96)			

Week 26 (n=41)	-0.9 (± 0.98)			
Week 30 (n=41)	-0.8 (± 1.05)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percent (%) Body Surface Area (BSA) at Each Visit

End point title	Change From Baseline in Percent (%) Body Surface Area (BSA) at Each Visit

End point description:

Percent BSA was calculated by modified rules of nines (pediatric subjects). Estimate were made from the following for a child up to the age of one year: head and neck total for front and back - 18%; thorax and abdomen-front -18%; thorax and abdomen-back - 18%; each upper limb total for front and back - 9%; each lower limb total for front and back - 14%. For over the age of one year, the relative percentage of BSA changes as follows: the head decreases by 1% per year and the lower limbs increase by 0.5% per year. By the age of ten years, the relative proportions assume the values for adult BSA as follows: perineum becomes 1%; each lower limb becomes a total of 18% front and back; head and neck become 9% total for front and back. Safety population included as all the subjects who have applied the study drug at least once. Here 'N' signifies number of subjects evaluable this outcome measure and 'n' signifies number of subjects evaluable for each time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 4, 8, 12, 20, 26 and 30 (Follow-up)

End point values	Calcitriol 3 mcg/g			
Subject group type	Reporting group			
Number of subjects analysed	51			
Units: Percent BSA				
arithmetic mean (standard deviation)				
Week 4 (n=51)	-1.3 (± 2.85)			
Week 8 (n=32)	-2.5 (± 4.03)			
Week 12 (n=49)	-3.4 (± 4.11)			
Week 20 (n=29)	-4.4 (± 4.61)			
Week 26 (n=41)	-3.9 (± 4.52)			
Week 30 (n=41)	-4.7 (± 5.91)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of treatment up to follow up (30 weeks)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups	
Reporting group title	Calcitriol 3 mcg/g

Reporting group description:

Subjects received calcitriol 3 mcg/g ointment twice daily without exceeding a maximum of 0.5 g/kg of body weight or 28 g daily (whichever was the lower) up to 26 weeks. Subjects were further followed up for 4 weeks.

Serious adverse events	Calcitriol 3 mcg/g		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 54 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Calcitriol 3 mcg/g		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 54 (16.67%)		
Skin and subcutaneous tissue disorders			
Skin Burning Sensation			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 54 (11.11%)		
occurrences (all)	6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 August 2014	Amendment 1: -Added Phase 3 designation for non-United States (US) regions -Updated contact information for the assigned medical expert -Added a 5-day time window to the baseline visit -Modified the wording for rolling over subjects from Study 18132 (EudraCT number 2014-001744-38) -Increased the rolling over period from 7 to 14 days -Corrected error in how the Subject Identification Number was allocated -Revised decision of performing 24-hour urine collection if calcium creatinine ratio was above normal range on a 4-hour fasting collection -Added that female subjects who began menses after Screening would be abstinent for the duration of the study or remain abstinent for at least 1 month after first use of a contraceptive to allow the contraceptive method to be effective -Added clarification of how to estimate BSA -Made minor editorial changes and added equivalent wording according to other non-US regions
02 December 2015	Amendment 2: -Added secondary objective of PK assessments in approximately 9 subjects aged 2 to 6 years and 11 months old with plaque psoriasis and a minimum of 3% BSA involvement, to fulfill FDA Phase 4 requirements -Added serum PD assessment at Baseline for subjects in the PK group in order to investigate PK/PD relationships -Changed the upper limit of age inclusion criterion from 17 years to 16 years 11 months at study start -Reduced the number of enrolled subjects -Removed requirement for equal distribution among age groups -Added blood draws at every study visit for subset of subjects in the PK group -Removed study visits at Week 8 and Week 20 -Removed text regarding subjects rolling over from Study 18132 (EudraCT number 2014-001744-38) -Instructions for use of topical anesthetic creams -Clarified the case management of PTH results that fell below the lower limit of normal -Added clarification of timing and location of study drug application in relation to PK blood sampling

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The trial was stopped due to slow enrollment and in agreement with the FDA. Full enrollment was never met in the study.

Notes: