EU Clinical Trials Register

Clinical trial results:
A two-part trial to evaluate the safety, tolerability, clinical effect and systemic exposure potential of topically applied GSK2981278 ointment in subjects with plaque psoriasis

Summary

EudraCT number	2016-002671-10
Trial protocol	DE
Global end of trial date	05 May 2017

Results information

Result version number	v3 (current)
This version publication date	31 January 2019
First version publication date	19 April 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	203820

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 December 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 May 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Part A: To evaluate the safety and tolerability of topically applied GSK2981278 and the systemic exposure of GSK2981278 following topical application in participants with plaque psoriasis. Part B: To evaluate the safety and tolerability of topically applied GSK2981278 and its vehicle and the clinical effect of topically applied GSK2981278 relative to vehicle control in participants with plaque psoriasis.

Protection of trial subjects:

To minimize the pain and discomfort associated with the punch biopsy procedure on the skin, local anesthesia was provided and the effect was checked by the physician before the procedure.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 February 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	6
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with chronic stable plaque psoriasis were recruited in this 2 part study to evaluate safety, tolerability and clinical effect of GSK2981278.

Pre-assignment

Screening details:

A total of 10 participants were screened; of which two were screen failures and eight were included in the treatment phase of Part A and received GSK2981278 4% ointment for 8 weeks. Part B of this study was not conducted as pre-defined efficacy criteria for continuing to Part B were not met. Hence no participants were enrolled in Part B.

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	GSK2981278 4%

Arm description:

Participants received 4% ointment of GSK2981278 twice daily for 8 weeks.

Arm type	Experimental
Investigational medicinal product name	GSK2981278
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

GSK2981278 ointment was administered topically as a thin layer to all affected areas of the skin, twice daily, for 8 weeks.

Number of subjects in period 1	GSK2981278 4%
Started	8
Completed	8

Baseline characteristics

Reporting groups

Reporting group title	GSK2981278 4%
Reporting group description:	
Participants received 4% ointment of GSK2981278 twice daily for 8 weeks.	

Reporting group values	GSK2981278 4%	Total	
Number of subjects	8	8	
Age categorical			
Units: Subjects			
All participants	8	8	
Age continuous			
Units: years			
arithmetic mean	54.9		
standard deviation	± 9.43	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	8	8	
Race/Ethnicity, Customized			
Units: Subjects			
White - White/Caucasian/European heritage	8	8	

End points

End points reporting groups

Reporting group title	GSK2981278 4%
Reporting group description:	
Participants received 4% ointment of GSK2981278 twice daily for 8 weeks.	

Primary: Number of participants with on-therapy serious adverse events (SAEs) and non-SAEs: Part A

End point title	Number of participants with on-therapy serious adverse events (SAEs) and non-SAEs: Part A[1]

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability, is a congenital anomaly/ birth defect, other situations and is associated with liver injury or impaired liver function. The analysis was performed on Safety analysis Population which comprised of all participants exposed to at least 1 application of study medication.

End point type	Primary

End point timeframe:

Up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[2]			
Units: Participants				
non-SAEs	1			
SAEs	0			

Notes:

[2] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with application site tolerability assessment score during treatment period: Part A

End point title	Number of participants with application site tolerability assessment score during treatment period: Part A[3]

End point description:

The investigator assessed application site tolerability focusing on the treated non-lesional skin surrounding the plaques at each visit using the 5-point tolerability assessment scale ranging from 0 (no intolerance) to 4 (very severe intolerance). Number of participants in the corresponding score at Day 1, 15, 29 and 57 has been presented.

End point type	Primary

End point timeframe:

Day 1, Day 15, Day 29, Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[4]			
Units: Participants				
Day 1; Grade 0	8			
Day 1; Grade 1	0			
Day 1; Grade 2	0			
Day 1; Grade 3	0			
Day 1; Grade 4	0			
Day 15; Grade 0	8			
Day 15; Grade 1	0			
Day 15; Grade 2	0			
Day 15; Grade 3	0			
Day 15; Grade 4	0			
Day 29; Grade 0	8			
Day 29; Grade 1	0			
Day 29; Grade 2	0			
Day 29; Grade 3	0			
Day 29; Grade 4	0			
Day 57; Grade 0	8			
Day 57; Grade 1	0			
Day 57; Grade 2	0			
Day 57; Grade 3	0			
Day 57; Grade 4	0			

Notes:

[4] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Negative Urinalysis Results: Part A

End point title	Number of Participants with Negative Urinalysis Results: Part

End point description:

Urine samples were collected from participants to evaluate urinalysis parameters including glucose, protein, erythrocytes and ketones. Number of participants with negative or normal urinalysis results at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values.

End point type	Primary

End point timeframe:

Up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[6]			
Units: Participants				
Glucose; Baseline	8			
Glucose; Day 15	8			
Glucose; Day 29	8			
Glucose; Day 57	8			
Protein; Baseline	8			
Protein; Day 15	8			
Protein; Day 29	8			
Protein; Day 57	8			
Erythrocytes; Baseline	8			
Erythrocytes; Day 15	8			
Erythrocytes; Day 29	8			
Erythrocytes; Day 57	8			
Ketones; Baseline	8			
Ketones; Day 15	8			
Ketones; Day 29	8			
Ketones; Day 57	8			

Notes:

[6] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Potential of hydrogen (pH) of urine: Part A

End point title	Change from Baseline in Potential of hydrogen (pH) of urine: Part A[7]

End point description:

The pH scale measures how acidic or basic a substance is. The pH scale ranges from 0 to 14. A pH of 7 is neutral. A pH less than 7 is acidic. A pH greater than 7 is basic. Urine samples were collected from participants and urine pH levels were assessed at Baseline, Day 15, Day 29 and Day 57. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[8]			
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Day 15	0.1 (± 0.83)			
Day 29	-0.1 (± 0.35)			
Day 57	-0.1 (± 0.35)			

Notes:

[8] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in specific gravity of urine: Part A

End point title	Change from Baseline in specific gravity of urine: Part A[9]

End point description:

Urine samples were collected from participants and specific gravity levels were assessed at Baseline, Day 15, Day 29 and Day 57. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[10]			
Units: Ratio				
arithmetic mean (standard deviation)				
Day 15	0.0019 (± 0.00799)			
Day 29	0.0019 (± 0.00530)			
Day 57	0.0025 (± 0.00707)			

Notes:

[10] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in blood urea nitrogen (BUN), glucose, potassium, sodium and calcium levels: Part A

End point title	Change from Baseline in blood urea nitrogen (BUN), glucose, potassium, sodium and calcium levels: Part A[11]

End point description:

Blood samples were collected from participants to evaluate clinical chemistry parameters including BUN, glucose, potassium, sodium and calcium. Change from Baseline in clinical chemistry parameters at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[12]			
Units: Millimoles per liter (Mmol/L)				
arithmetic mean (standard deviation)				
BUN; Day 15	-0.2678 (± 1.23300)			
BUN; Day 29	-0.3570 (± 0.42670)			
BUN; Day 57	0.4909 (± 1.40146)			
Glucose; Day 15	0.041632 (± 0.7296677)			
Glucose; Day 29	0.104081 (± 0.7258495)			
Glucose; Day 57	0.298366 (± 0.4163911)			
Potassium; Day 15	-0.14 (± 0.272)			
Potassium; Day 29	0.00 (± 0.312)			
Potassium; Day 57	0.13 (± 0.328)			
Sodium; Day 15	-1.1 (± 2.17)			
Sodium; Day 29	0.8 (± 2.25)			
Sodium; Day 57	-0.4 (± 1.06)			
Calcium; Day 15	0.021 (± 0.0624)			
Calcium; Day 29	0.038 (± 0.0765)			
Calcium; Day 57	-0.013 (± 0.0886)			

Notes:

[12] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in creatinine, total and direct bilirubin levels: Part A

End point title	Change from Baseline in creatinine, total and direct bilirubin levels: Part A[13]

End point description:

Blood samples were collected from participants to evaluate clinical chemistry parameters including

creatinine, total and direct bilirubin. Change from Baseline in clinical chemistry parameters at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[14]			
Units: Micromoles per liter (µmol/L)				
arithmetic mean (standard deviation)				
Creatinine; Day 15	-5.8565 (± 2.16212)			
Creatinine; Day 29	-3.8675 (± 6.32075)			
Creatinine; Day 57	-3.7570 (± 6.92444)			
Total bilirubin; Day 15	1.425 (± 2.7396)			
Total bilirubin; Day 29	1.995 (± 2.5171)			
Total bilirubin; Day 57	-0.342 (± 1.4307)			
Direct bilirubin; Day 15	0.3705 (± 0.66154)			
Direct bilirubin; Day 29	0.3990 (± 0.79963)			
Direct bilirubin; Day 57	0.0000 (± 0.52706)			

Notes:

[14] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase levels: Part A

End point title	Change from Baseline in aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase levels: Part A[15]

End point description:

Blood samples were collected from participants to evaluate clinical chemistry parameters including AST, ALT and alkaline phosphatase. Change from Baseline in clinical chemistry parameters at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[16]			
Units: International unit per liter (IU/L)				
arithmetic mean (standard deviation)				
AST; Day 15	1.3 (± 4.43)			
AST; Day 29	-0.3 (± 2.92)			
AST; Day 57	-0.3 (± 6.23)			
ALT; Day 15	2.8 (± 8.75)			
ALT; Day 29	0.6 (± 5.26)			
ALT; Day 57	2.0 (± 8.59)			
Alkaline phosphatase; Day 15	2.1 (± 5.87)			
Alkaline phosphatase; Day 29	2.9 (± 12.89)			
Alkaline phosphatase; Day 57	-0.8 (± 11.80)			

Notes:

[16] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in protein and albumin levels: Part A

End point title	Change from Baseline in protein and albumin levels: Part A[17]

End point description:

Blood samples were collected from participants to evaluate clinical chemistry parameters including protein and albumin. Change from Baseline in clinical chemistry parameters at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[18]			
Units: Grams per liter (g/L)				
arithmetic mean (standard deviation)				
Protein; Day 15	1.9 (± 2.90)			
Protein; Day 29	-1.4 (± 2.83)			
Protein; Day 57	1.8 (± 3.65)			
Albumin; Day 15	1.4 (± 1.92)			
Albumin; Day 29	1.3 (± 1.67)			

Albumin; Day 57	1.0 (± 2.56)

Notes:

[18] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in platelet, leukocyte, neutrophils, lymphocytes, monocytes, eosinophils and basophils levels: Part A

End point title	Change from Baseline in platelet, leukocyte, neutrophils, lymphocytes, monocytes, eosinophils and basophils levels: Part A[19]

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including platelets, leukocytes, neutrophils, lymphocytes, monocytes, eosinophils and basophils. Change from Baseline in clinical hematology parameters at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[20]			
Units: 10^9 cells/L				
arithmetic mean (standard deviation)				
Platelet; Day 15	-3.6 (± 50.90)			
Platelet; Day 29	-1.0 (± 28.98)			
Platelet; Day 57	0.1 (± 25.31)			
Leukocytes; Day 15	0.76 (± 2.745)			
Leukocytes; Day 29	0.42 (± 0.910)			
Leukocytes; Day 57	0.35 (± 0.780)			
Neutrophils; Day 15	0.695 (± 2.7477)			
Neutrophils; Day 29	0.144 (± 1.1659)			
Neutrophils; Day 57	0.217 (± 0.4432)			
Lymphocytes; Day 15	-0.019 (± 0.6335)			
Lymphocytes; Day 29	0.243 (± 0.4457)			
Lymphocytes; Day 57	0.151 (± 0.3756)			
Monocytes; Day 15	0.090 (± 0.2778)			

Monocytes; Day 29	-0.040 (± 0.2099)		
Monocytes; Day 57	-0.063 (± 0.2344)		
Eosinophils; Day 15	0.019 (± 0.1579)		
Eosinophils; Day 29	0.085 (± 0.1321)		
Eosinophils; Day 57	0.029 (± 0.0825)		
Basophils; Day 15	-0.008 (± 0.0287)		
Basophils; Day 29	0.001 (± 0.0264)		
Basophils; Day 57	0.004 (± 0.0151)		

Notes:

[20] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in erythrocyte levels: Part A

End point title	Change from Baseline in erythrocyte levels: Part A[21]

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including erythrocytes. Change from Baseline in clinical hematology parameters at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[22]			
Units: 10^12 cells/L				
arithmetic mean (standard deviation)				
Day 15	0.013 (± 0.2042)			
Day 29	0.055 (± 0.2555)			
Day 57	0.061 (± 0.2785)			

Notes:

[22] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hemoglobin levels: Part A

End point title	Change from Baseline in hemoglobin levels: Part A[23]

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including hemoglobin. Change from Baseline in clinical hematology parameters at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[24]			
Units: g/L				
arithmetic mean (standard deviation)				
Day 15	1.3 (± 6.18)			
Day 29	2.6 (± 7.63)			
Day 57	1.5 (± 9.18)			

Notes:

[24] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in hematocrit levels: Part A

End point title	Change from Baseline in hematocrit levels: Part A[25]

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including hematocrit. Change from Baseline in clinical hematology parameters at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

Notes:

[25] - 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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[26]			
Units: Proportion of Red blood cells in blood				
arithmetic mean (standard deviation)				
Day 15	0.0040 (± 0.01752)			
Day 29	0.0090 (± 0.02203)			
Day 57	0.0076 (± 0.02628)			

Notes:

[26] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in mean corpuscular volume (MCV) levels: Part A

End point title	Change from Baseline in mean corpuscular volume (MCV) levels: Part A[27]

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including MCV. Change from Baseline in clinical hematology parameters at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

Notes:

[27] - 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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[28]			
Units: Femtoliter (fL)				
arithmetic mean (standard deviation)				
Day 15	0.46 (± 1.235)			
Day 29	0.86 (± 1.112)			
Day 57	0.34 (± 1.172)			

Notes:

[28] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in mean corpuscular hemoglobin (MCH) levels: Part A

End point title	Change from Baseline in mean corpuscular hemoglobin (MCH) levels: Part A[29]

End point description:

Blood samples were collected from participants to evaluate clinical hematology parameters including MCH. Change from Baseline in clinical hematology parameters at Day 15, Day 29 and Day 57 are presented. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

Notes:

[29] - 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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[30]			
Units: Picograms (Pg)				
arithmetic mean (standard deviation)				
Day 15	0.16 (± 0.325)			
Day 29	0.21 (± 0.253)			
Day 57	-0.06 (± 0.421)			

Notes:

[30] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels: Part A

End point title	Change from Baseline in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels: Part A[31]

End point description:

Vital sign measurements including SBP and DBP were taken in a seated or supine position after 5-minutes of rest. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

Notes:

[31] - 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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[32]			
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP; Day 15	-1.9 (± 4.58)			
SBP; Day 29	-2.5 (± 4.63)			
SBP; Day 57	-2.5 (± 2.67)			
DBP; Day 15	0.0 (± 2.67)			
DBP; Day 29	1.3 (± 4.43)			
DBP: Day 57	0.6 (± 4.17)			

Notes:

[32] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in pulse rate levels: Part A

End point title	Change from Baseline in pulse rate levels: Part A[33]

End point description:

Vital sign measurements including pulse rate were taken in a seated or supine position after 5-minutes of rest. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value.

End point type	Primary

End point timeframe:

Baseline and up to Day 57

Notes:

[33] - 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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[34]			
Units: Beats per minute				
arithmetic mean (standard deviation)				
Day 15	3.3 (± 9.19)			
Day 29	0.3 (± 12.21)			
Day 57	1.3 (± 11.36)			

Notes:

[34] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in Electrocardiogram (ECG) parameters including single RR heart rate: Part A

End point title	Change from Baseline in Electrocardiogram (ECG) parameters

End point description:

Single measurements of 12-lead ECG were obtained using an ECG machine to measure RR heart rate. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value

End point type	Primary

End point timeframe:

Baseline and up to Day 57

Notes:

[35] - 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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[36]			
Units: Beats per minute				
arithmetic mean (standard deviation)				
Day 29	-2.5 (± 16.81)			
Day 57	-3.5 (± 12.42)			

Notes:

[36] - Safety analysis Population

Statistical analyses

No statistical analyses for this end point

Primary: Change from Baseline in ECG parameters including PR interval, QRS duration, QT interval, Corrected QT interval using Bazett's formula (QTcB) and RR interval: Part A

End point title	Change from Baseline in ECG parameters including PR interval, QRS duration, QT interval, Corrected QT interval using Bazett's formula (QTcB) and RR interval: Part A[37]

End point description:

Single measurements of 12-lead ECG were obtained using an ECG machine to measure PR interval, QRS duration, QT interval, QTcB and RR interval. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value

End point type	Primary

End point timeframe:

Baseline and up to Day 57

Notes:

[37] - 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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Milliseconds (msec)				
arithmetic mean (standard deviation)				
PR interval; Day 29	-0.5 (± 9.78)			
PR interval; Day 57	7.3 (± 12.78)			

QRS duration; Day 29	-0.5 (± 4.24)
QRS duration; Day 57	-0.3 (± 2.92)
QT interval; Day 29	12.8 (± 28.88)
QT interval; Day 57	9.0 (± 28.57)
QTcB interval; Day 29	10.0 (± 15.62)
QTcB interval; Day 57	3.5 (± 15.96)
RR interval; Day 29	9.5 (± 170.62)
RR interval; Day 57	13.0 (± 124.12)

Statistical analyses

No statistical analyses for this end point

Primary: Plasma concentration of GSK2981278 at nominal time: Part A

End point title	Plasma concentration of GSK2981278 at nominal time: Part

End point description:

Blood samples were collected at indicated time points for pharmacokinetic (PK) analysis of GSK2981278. Non-quantifiable values in a profile occurring before the first measurable concentration were assigned a value of zero concentration. Single non-quantifiable values occurring between measurable concentrations in a profile were omitted. The analysis was performed on PK analysis Population which comprised of participants with at least one sample collected and analyzed for plasma drug concentration. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Primary

End point timeframe:

Pre-dose, 1, 2, 4, 6, 8, 10 hours post-dose on Day 1, Day 29 and Day 57; Pre-dose, 2 hours post-dose on Day 15

Notes:

[38] - 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: There are no statistical data to report.

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[39]			
Units: Picograms per milliliter (Pg/mL)				
arithmetic mean (standard deviation)				
Pre-dose; Day 1; n= 8	0.00 (± 0.000)			
1 hour post-dose; Day 1; n= 8	151.89 (± 210.535)			
2 hours post-dose; Day 1; n= 8	281.54 (± 589.927)			
4 hours post-dose; Day 1; n= 8	171.38 (± 160.357)			
6 hours post-dose; Day 1; n= 8	610.73 (± 1141.415)			
8 hours post-dose; Day 1; n= 8	192.06 (± 168.443)			
10 hours post-dose; Day 1; n= 8	554.94 (± 828.825)			
Pre-dose; Day 15; n= 7	1203.71 (± 1203.796)			

2 hours post-dose; Day 15; n= 8	893.00 (± 737.610)				
Pre-dose; Day 29; n= 8	1122.00 (± 587.760)				
1 hour post-dose; Day 29; n= 8	1299.63 (± 910.793)				
2 hours post-dose; Day 29; n= 8	1062.38 (± 662.050)				
4 hours post-dose; Day 29; n= 8	769.38 (± 369.861)				
6 hours post-dose; Day 29; n= 8	1022.63 (± 720.269)				
8 hours post-dose; Day 29; n= 7	897.71 (± 325.169)				
10 hours post-dose; Day 29; n= 8	875.38 (± 584.879)				
Pre-dose; Day 57; n= 8	875.75 (± 707.446)				
1 hour post-dose; Day 57; n= 8	1273.75 (± 784.902)				
2 hours post-dose; Day 57; n= 8	1077.00 (± 1128.070)				
4 hours post-dose; Day 57; n= 8	758.13 (± 494.661)				
6 hours post-dose; Day 57; n= 8	760.38 (± 550.695)				
8 hours post-dose; Day 57; n= 8	809.13 (± 373.947)				
10 hours post-dose; Day 57; n= 8	841.25 (± 579.772)				

Notes:

[39] - PK analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean percent change from Baseline in target plaque severity score (TPSS): Part A

End point title	Mean percent change from Baseline in target plaque severity score (TPSS): Part A

End point description:

The TPSS is the measure of clinical effect of GSK2981278. A target lesion of at least 9 centimeter square (cm^2) with a TPSS >=5 and an induration sub score >=2 was selected at Baseline. TPSS Total score was calculated by adding the individual scores of erythema, scaling, and induration (plaque thickness), assessed by the investigator on a 5-point scale ranging from 0=none to 4=very marked. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value. Percent change from Baseline was calculated by dividing change from Baseline value by Baseline value and multiplying it by 100. The analysis was performed on per protocol (PP) analysis Population which comprised of all participants eligible for treatment phase and who comply closely with the protocol.

End point type	Secondary

End point timeframe:

Baseline and up to Week 8

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[40]			
Units: Percent change				
arithmetic mean (standard deviation)				
Day 15	-6.5 (± 7.24)			
Day 29	-3.0 (± 5.74)			
Day 57	-4.3 (± 10.61)			

Notes:

[40] - PP analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean percent change from Baseline in Physician's Global Assessment (PGA) score: Part A

End point title	Mean percent change from Baseline in Physician's Global Assessment (PGA) score: Part A

End point description:

The PGA is a clinical tool for assessing the current state/severity of a participant's psoriasis. It is a static 5-point morphological assessment of overall disease severity, as determined by the investigator, using the clinical characteristics of erythema, plaque thickness, and scaling as guidelines. The 5-point scale ranges from 0=clear to 4=severe. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value. Percent change from Baseline was calculated by dividing change from Baseline value by Baseline value and multiplying it by 100.

End point type	Secondary

End point timeframe:

Baseline and up to Week 8

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[41]			
Units: Percent change				
arithmetic mean (standard deviation)				
Day 15	-3.1 (± 8.84)			
Day 29	-3.1 (± 8.84)			
Day 57	0.0 (± 0.0)			

Notes:

[41] - PP analysis Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean percent change from Baseline in Psoriasis Area and Severity Index (PASI) score: Part A

End point title	Mean percent change from Baseline in Psoriasis Area and

| | Severity Index (PASI) score: Part A |

End point description:

The PASI is a standard tool for assessing the severity of psoriasis that considers the overall severity of erythema, thickness, and scale, as well as the extent of body surface area (BSA) affected with psoriasis. The 3 clinical signs are each graded on a 5-point scale (0=none to 4=severe) and the percent BSA affected is scored on a 7-point scale (0= 0% skin with psoriasis to 6=>=90% skin with psoriasis) for each of the 4 specified body regions. The individual scores are multiplied by a weighted factor for each body region; the sum of these scores gives the overall PASI score. Higher scores indicate more severe disease. Last observation values collected prior to the first application of study treatment were considered as Baseline values. Change from Baseline was calculated as post-Baseline visit values minus Baseline value. Percent change from Baseline was calculated by dividing change from Baseline value by Baseline value and multiplying it by 100.

End point type	Secondary

End point timeframe:

Baseline and up to Week 8

End point values	GSK2981278 4%			
Subject group type	Reporting group			
Number of subjects analysed	8[42]			
Units: Percent change				
arithmetic mean (standard deviation)				
Day 15	-3.98 (± 10.459)			
Day 29	-0.27 (± 4.058)			
Day 57	4.26 (± 7.119)			

Notes:

[42] - PP analysis Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:	
On-therapy SAEs and non-SAEs are presented from the start of study treatment up to Day 57.	
Adverse event reporting additional description:	
On-therapy SAEs and non-serious AEs are reported for members of the Safety analysis Population	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	GSK2981278 4%
Reporting group description:	
Participants received 4% ointment of GSK2981278 twice daily for 8 weeks.	

Serious adverse events	GSK2981278 4%		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	GSK2981278 4%		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)		
Infections and infestations			
COMMON COLD			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2016	1. Psoriasis Symptom Diary revised to the original published version 2. Clarification of intent for urine sample analysis, minor text changes to Part A and B Time and Events tables to ensure consistency, and more comprehensive information on the allergic reaction risk.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported