Clinical trial results:
A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of JTE-451 Administered for 16 Weeks in Subjects with Moderate to Severe Plaque Psoriasis (IMPACT-PS)

Summary

EudraCT number	2018-003359-40
Trial protocol	PL
Global end of trial date	13 March 2020

Results information

Result version number	v1 (current)
This version publication date	20 March 2021
First version publication date	20 March 2021

Trial information

Trial identification

Sponsor protocol code	AE451-G-18-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03832738
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 129963

Notes:

Sponsors

Sponsor organisation name	Akros Pharma Inc.
Sponsor organisation address	302 Carnegie Center, Suite 300, Princeton, United States, NJ 08540
Public contact	Kala Patel, Akros Pharma Inc., patel@akrospharma.com
Scientific contact	Kala Patel, Akros Pharma Inc., patel@akrospharma.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	20 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 March 2020
Global end of trial reached?	Yes
Global end of trial date	13 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was a Phase-2, multicentre, double-blind, placebo-controlled 16-week study.

The primary objective of this study was to evaluate the efficacy of JTE-451 administered for 16 weeks in subjects with moderate to severe plaque psoriasis compared with placebo.

The secondary objectives of the study were to evaluate the safety, tolerability and pharmacokinetics (PK) of JTE-451 administered for 16 weeks in subjects with moderate to severe plaque psoriasis.

Protection of trial subjects:

The study was conducted in compliance with the protocol, Good Clinical Practice and applicable regulatory requirement(s) (e.g., 21 Code of Federal Regulations Parts 50, 56, 312 in the United States), Sponsor/designee policies and procedures, and all applicable local and national clinical trial regulations.

From a safety perspective, appropriate study restrictions based on the mechanism of action (MOA) of JTE-451 (i.e., selective immunomodulatory effect) were implemented including screening procedures and exclusion criteria to mitigate and minimise the risk of infections as well as tuberculosis and viral infections were included to ensure the safety of subjects. Each subject signed an informed consent form (ICF) containing appropriate trial and study drug information and was provided a copy of the ICF.

The subjects at high risk of developing immunosuppression-related adverse events (AEs), such as infections or malignancies, including those with pre-existing conditions (e.g., clinically-manifested or active tubercle bacillus (TB)/untreated latent TB, active infections with hepatitis B virus, hepatitis C virus or human immunodeficiency virus or significant haematological condition were excluded from participating in the study. Other general safety-related restrictions such as cardiovascular-system-related, hepatic, and renal function-related restrictions, as well as the known safety signals associated with other compounds with similar MOA, were implemented to monitor and adequately manage safety-related findings.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 January 2019
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	Poland: 124
Country: Number of subjects enrolled	United States: 15
Country: Number of subjects enrolled	Canada: 13

Worldwide total number of subjects	152
EEA total number of subjects	124

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)	139
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible subjects were randomised at Visit 2 to receive JTE-451 200 mg twice daily (BID; 400 mg/day), 400 mg BID (800 mg/day), or placebo BID for 16 weeks. Randomisation was stratified based on prior exposure of subjects to biologic therapy (biologic-naïve versus [vs.] biologic-experienced) and body weight (<90 kg vs. ≥90 kg at Visit 2).

Pre-assignment

Screening details:

Study duration was approximately 24 weeks per subject as follows:
• Screening period: Day -28 (Visit 1) to Day 1 (Visit 2/Randomisation Visit)
• 16-week double-blind treatment period: Day 1 (Visit 2) to Day 112±4 (Visit 7/Week 16)
• Up to 4-week follow-up period: Day 112±4 (Visit 7/Week 16) to Day 140±4 (Visit 8/Week 20)

Period 1

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

Blinding implementation details:

The treatment assigned to each subject was not disclosed to the Sponsor members or designees involved in the study, study staff at the site or to the subject. JTE-451 200 mg tablets as well as placebo tablets were supplied as unbranded tablets, which were identical in appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	JTE-451 200 mg BID

Arm description:

The subjects received a total daily dose of 400 mg of JTE-451.

Arm type	Experimental
Investigational medicinal product name	JTE-451 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

During the treatment period, the subjects self-administered 2 oral doses (2 tablets [1 tablet of JTE-451 200 mg and 1 placebo tablet]/dose, BID at approximately 12-hour intervals, regardless of meals) on Day 1 and daily up to Week 16.

Each JTE-451 tablet contained 200 mg of JTE-451 and inactive ingredients. Each placebo tablet contained the same inactive ingredients as JTE-451 200 mg tablet except the active drug (JTE-451).

Arm title	JTE-451 400 mg BID

Arm description:

The subjects received a total daily dose of 800 mg of JTE-451.

Arm type	Experimental
Investigational medicinal product name	JTE-451 200 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

During the treatment period, the subjects self-administered 2 oral doses (2 tablets of JTE-451 200 mg/dose, BID at approximately 12-hour intervals, regardless of meals) on Day 1 and daily up to Week 16.

Each JTE-451 tablet contained 200 mg of JTE-451 and inactive ingredients.

Arm title	Placebo

Arm description:

The subjects received a placebo-treatment.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

During the treatment period, the subjects self-administered 2 oral doses (2 placebo tablets/dose, BID at approximately 12-hour intervals, regardless of meals) on Day 1 and daily up to Week 16.

Each placebo tablet contained the same inactive ingredients as JTE-451 200 mg tablet except the active drug (JTE-451).

Number of subjects in period 1	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo
Started	51	50	51
Completed	43	38	32
Not completed	8	12	19
Consent withdrawn by subject	6	7	16
Physician decision	-	1	2
Adverse event, non-fatal	2	3	1
Pregnancy	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	JTE-451 200 mg BID
Reporting group description:	
The subjects received a total daily dose of 400 mg of JTE-451.	
Reporting group title	JTE-451 400 mg BID
Reporting group description:	
The subjects received a total daily dose of 800 mg of JTE-451.	
Reporting group title	Placebo
Reporting group description:	
The subjects received a placebo-treatment.	

Reporting group values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo
Number of subjects	51	50	51
Age categorical			
Demographic details analysed for Intent-to-Treat (ITT) population are presented here. The ITT population consisted of all subjects who were randomised at Visit 2.			
Units: Subjects			
Adults (18-64 years)	47	46	46
From 65-84 years	4	4	5
Age continuous			
Units: years			
arithmetic mean	45.7	45.5	44.5
standard deviation	± 12.33	± 13.96	± 13.08
Gender categorical			
Units: Subjects			
Female	13	21	16
Male	38	29	35
Weight category at randomisation			
Units: Subjects			
<90 kg	25	24	25
≥90 kg	26	26	26
Screening body mass index			
Units: kilogram(s)/square meter			
arithmetic mean	28.843	29.828	29.519
standard deviation	± 5.1080	± 5.2058	± 4.1446

Reporting group values	Total		
Number of subjects	152		
Age categorical			
Demographic details analysed for Intent-to-Treat (ITT) population are presented here. The ITT population consisted of all subjects who were randomised at Visit 2.			
Units: Subjects			
Adults (18-64 years)	139		
From 65-84 years	13		
Age continuous			
Units: years			
arithmetic mean			

standard deviation	-		

Gender categorical Units: Subjects			
Female	50		
Male	102		
Weight category at randomisation Units: Subjects			
<90 kg	74		
≥90 kg	78		
Screening body mass index Units: kilogram(s)/square meter arithmetic mean standard deviation	 -		

End points

End points reporting groups

Reporting group title	JTE-451 200 mg BID
Reporting group description:	
The subjects received a total daily dose of 400 mg of JTE-451.	
Reporting group title	JTE-451 400 mg BID
Reporting group description:	
The subjects received a total daily dose of 800 mg of JTE-451.	
Reporting group title	Placebo
Reporting group description:	
The subjects received a placebo-treatment.	
Subject analysis set title	JTE-451 200 mg BID - PK Population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The PK population consisted of the randomised subjects who received at least one dose of JTE-451 and had at least one usable JTE-451 plasma concentration measurement. In JTE-451 200 mg BID - PK Population, the numbers of subjects analysed were 49 at Week 0 (pre-dose), 45 at Week 4 (pre-dose), 41 at Week 8 (pre-dose), 42 at Week 12 (pre-dose), and 42 at Week 16 (trough).	
Subject analysis set title	JTE-451 400 mg BID - PK Population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The PK population consisted of the randomised subjects who received at least one dose of JTE-451 and had at least one usable JTE-451 plasma concentration measurement. In JTE-451 400 mg BID - PK Population, the numbers of subjects analysed were 47 at Week 0 (pre-dose), 43 at Week 4 (pre-dose), 39 at Week 8 (pre-dose), 36 at Week 12 (pre-dose), and 33 at Week 16 (trough).	

Primary: Proportion of subjects who achieved psoriasis area and severity index (PASI)-75 response rate at end of treatment (EOT) in the ITT population

End point title	Proportion of subjects who achieved psoriasis area and severity index (PASI)-75 response rate at end of treatment (EOT) in the ITT population
End point description:	
The PASI quantifies the severity of a subject's psoriasis based on both, "lesion severity" and the "percent of body surface area (BSA)" affected. PASI is a composite scoring by the investigator of degree of erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk [including axillae and groin], and lower limbs [including buttocks]), with adjustment for the percent of BSA involved for each body region and for the proportion of the body region to the whole body. The PASI score can vary in increments of 0.1 and range from 0.0 to 72.0, with higher scores representing greater severity of psoriasis. PASI-75 response rate was defined as at least 75 percent (%) reduction in PASI score relative to Baseline.	
End point type	Primary
End point timeframe:	
EOT	

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	51	
Units: number of subjects	6	11	4	

Statistical analyses

Statistical analysis title	Analysis of PASI-75 response rate at EOT
Comparison groups	JTE-451 200 mg BID v Placebo
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.558 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	5.8

Notes:

[1] - The p-value was estimated based on Cochran-Mantel-Haenszel test stratified by prior exposure to biologic therapy (Yes/No) and body weight (<90 kg/≥90 kg).

Statistical analysis title	Analysis of PASI-75 response rate at EOT
Comparison groups	JTE-451 400 mg BID v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.035 [2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	13.1

Notes:

[2] - The p-value was estimated based on Cochran-Mantel-Haenszel test stratified by prior exposure to biologic therapy (Yes/No) and body weight (<90 kg/≥90 kg).

Secondary: Proportion of subjects who achieved PASI-50 response rate at EOT in the ITT population

End point title	Proportion of subjects who achieved PASI-50 response rate at EOT in the ITT population

End point description:

The PASI quantifies the severity of a subject's psoriasis based on both, "lesion severity" and the "percent of BSA" affected. PASI is a composite scoring by the investigator of degree of erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk [including axillae and groin], and lower limbs [including buttocks]), with adjustment for the percent of BSA involved for each body region and for the proportion of the body region to the whole

body. The PASI score can vary in increments of 0.1 and range from 0.0 to 72.0, with higher scores representing greater severity of psoriasis. PASI-50 response rate was defined as at least 50% reduction in PASI score relative to Baseline.

End point type	Secondary

End point timeframe:

EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	51	
Units: number of subjects	17	21	9	

Statistical analyses

Statistical analysis title	Analysis of PASI-50 response rate at EOT
Comparison groups	JTE-451 200 mg BID v Placebo
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.086 [3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	5.75

Notes:

[3] - The p-value was estimated based on Cochran-Mantel-Haenszel test stratified by prior exposure to biologic therapy (Yes/No) and body weight (<90 kg/≥90 kg).

Statistical analysis title	Analysis of PASI-50 response rate at EOT
Comparison groups	JTE-451 400 mg BID v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.45
upper limit	9.75

Notes:

[4] - The p-value was estimated based on Cochran-Mantel-Haenszel test stratified by prior exposure to biologic therapy (Yes/No) and body weight (<90 kg/≥90 kg).

Secondary: Proportion of subjects who achieved PASI-90 response rate at EOT in the ITT population

End point title	Proportion of subjects who achieved PASI-90 response rate at EOT in the ITT population

End point description:

The PASI quantifies the severity of a subject's psoriasis based on both, "lesion severity" and the "percent of BSA" affected. PASI is a composite scoring by the investigator of degree of erythema, induration, and scaling (each scored separately) for each of 4 body regions (head and neck, upper limbs, trunk [including axillae and groin], and lower limbs [including buttocks]), with adjustment for the percent of BSA involved for each body region and for the proportion of the body region to the whole body. The PASI score can vary in increments of 0.1 and range from 0.0 to 72.0, with higher scores representing greater severity of psoriasis. PASI-90 response rate was defined as at least 90% reduction in PASI score relative to Baseline.

End point type	Secondary

End point timeframe:

EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	51	
Units: number of subjects	1	3	1	

Statistical analyses

Statistical analysis title	Analysis of PASI-90 response rate at EOT
Comparison groups	Placebo v JTE-451 200 mg BID
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.999 [5]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	17.25

Notes:

[5] - The p-value was estimated based on Cochran-Mantel-Haenszel test stratified by prior exposure to biologic therapy (Yes/No) and body weight (<90 kg/≥90 kg).

Statistical analysis title	Analysis of PASI-90 response rate at EOT
Comparison groups	JTE-451 400 mg BID v Placebo

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.244 [6]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	41.2

Notes:

[6] - The p-value was estimated based on Cochran-Mantel-Haenszel test stratified by prior exposure to biologic therapy (Yes/No) and body weight (<90 kg/≥90 kg).

Secondary: Percent change from baseline in PASI score at EOT in the ITT population

End point title	Percent change from baseline in PASI score at EOT in the ITT population

End point description:

Combined assessment of lesion severity and area affected into single score; range=0 (no disease) to 72 (maximal disease). Body divided into 4 sections=head, upper/lower limbs, trunk; each area scored by itself and scores combined for final PASI. For each section, percent area of skin involved was estimated: 0 (0%) to 6 (90-100%) and severity estimated by clinical signs of erythema, induration, scaling; ranged 0-4: 0=none, 1=slight, 2=moderate, 3=marked, 4=very marked. Final PASI=sum of severity parameters for each section*area score*weighing factor (head=0.1, upper limbs=0.2, trunk=0.3, lower limbs=0.4); total possible score range: 0=no disease to 72=maximal disease.

End point type	Secondary

End point timeframe:

Baseline and EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	48	
Units: percent				
arithmetic mean (standard deviation)	-30.33 (± 40.971)	-37.89 (± 37.896)	-17.53 (± 34.701)	

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects who achieved Static Physician’s Global Assessment (sPGA) score of 0 or 1 at EOT in the ITT population

End point title	Proportion of subjects who achieved Static Physician’s Global Assessment (sPGA) score of 0 or 1 at EOT in the ITT population

End point description:

The sPGA of psoriasis is scored on a 5-point scale, reflecting a global consideration of the erythema, induration, and scaling across all psoriatic lesions. Average erythema, induration, and scaling are scored

separately over the whole body according to a 5-point severity scale (0 [no symptom] to 4 [severe symptom]). The total score was calculated as average of the 3 severity scores and rounded to the nearest whole number score to determine the sPGA score and category (0=cleared; 1=minimal; 2=mild; 3=moderate; and 4=severe). sPGA response was defined as 0 (clear) or 1 (minimal).

End point type	Secondary

End point timeframe:

EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	51	
Units: number of subjects	13	14	3	

Statistical analyses

Statistical analysis title	Analysis of subjects with sPGA score 0 or 1 at EOT
Comparison groups	JTE-451 200 mg BID v Placebo
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 [7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	5.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	19.62

Notes:

[7] - The p-value was estimated based on Cochran-Mantel-Haenszel test stratified by prior exposure to biologic therapy (Yes/No) and body weight (<90 kg/≥90 kg).

Statistical analysis title	Analysis of subjects with sPGA score 0 or 1 at EOT
Comparison groups	JTE-451 400 mg BID v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	7.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.86
upper limit	29.08

Notes:

[8] - The p-value was estimated based on Cochran-Mantel-Haenszel test stratified by prior exposure to biologic therapy (Yes/No) and body weight (<90 kg/≥90 kg).

Secondary: Change from baseline in sPGA score at EOT in the ITT population

End point title	Change from baseline in sPGA score at EOT in the ITT population

End point description:

The sPGA of psoriasis is scored on a 5-point scale, reflecting a global consideration of the erythema, induration, and scaling across all psoriatic lesions. Average erythema, induration, and scaling are scored separately over the whole body according to a 5-point severity scale (0 [no symptom] to 4 [severe symptom]). The total score was calculated as average of the 3 severity scores and rounded to the nearest whole number score to determine the sPGA score and category (0=cleared; 1=minimal; 2=mild; 3=moderate; and 4=severe).

End point type	Secondary

End point timeframe:

Baseline and EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	48	
Units: units on scale				
arithmetic mean (standard deviation)	-0.96 (± 0.848)	-1.02 (± 0.869)	-0.54 (± 0.713)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change from baseline in psoriasis BSA at EOT in the ITT population

End point title	Percent change from baseline in psoriasis BSA at EOT in the ITT population

End point description:

The total BSA affected by plaque-type psoriasis was estimated from the percentages of areas affected, including head, trunk, upper limbs and lower limbs. Each reported percentage was multiplied by its respective body region corresponding factor (head=0.1, upper limbs=0.2, trunk=0.3, lower limbs=0.4) and the resulting 4 values were added up to estimate the total BSA affected by plaque-type psoriasis.

End point type	Secondary

End point timeframe:

Baseline and EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	48	
Units: percent				
arithmetic mean (standard deviation)	-18.67 (± 39.582)	-19.03 (± 48.696)	-5.74 (± 38.707)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Skindex-16 Overall Score at EOT in the ITT population

End point title	Change from baseline in Skindex-16 Overall Score at EOT in the ITT population

End point description:

Skindex-16 questionnaire contains 16 questions related to quality of life in subjects with skin disease. It consists of a short 16-item assessment completed by the subject, with each item rated on a 7-point Likert scale (0=never bothered to 6=always bothered). Responses to the Skindex-16 are categorised into three subscales: symptom, emotional, and functional; and their respective scores are expressed in a linear scale from 0 (no effect) to 100 (effect experienced all the time). Overall scale score is an average of 16 items.

End point type	Secondary

End point timeframe:

Baseline and EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	48	
Units: units on scale				
arithmetic mean (standard deviation)	-10.029 (± 23.2635)	-10.896 (± 26.7910)	-3.386 (± 20.8617)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Skindex-16 Symptom Scale Scores at EOT in the ITT population

End point title	Change from baseline in Skindex-16 Symptom Scale Scores at EOT in the ITT population

End point description:

Skindex-16 questionnaire contains 16 questions related to quality of life in subjects with skin disease. It consists of a short 16-item assessment completed by the subject, with each item rated on a 7-point Likert scale (0=never bothered to 6=always bothered). Responses to the Skindex-16 are categorised into three subscales: symptom, emotional, and functional; and their respective scores are expressed in a linear scale from 0 (no effect) to 100 (effect experienced all the time). Symptom scale score is an

average of items 1 to 4.

End point type	Secondary

End point timeframe:

Baseline and EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	48	
Units: units on scale				
arithmetic mean (standard deviation)	-8.905 (± 34.2989)	-11.500 (± 31.5148)	-2.170 (± 26.0563)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Skindex-16 Emotions Scale Scores at EOT in the ITT population

End point title	Change from baseline in Skindex-16 Emotions Scale Scores at EOT in the ITT population

End point description:

Skindex-16 questionnaire contains 16 questions related to quality of life in subjects with skin disease. It consists of a short 16-item assessment completed by the subject, with each item rated on a 7-point Likert scale (0=never bothered to 6=always bothered). Responses to the Skindex-16 are categorised into three subscales: symptom, emotional, and functional; and their respective scores are expressed in a linear scale from 0 (no effect) to 100 (effect experienced all the time). Emotions scale score is an average of items 5 to 11.

End point type	Secondary

End point timeframe:

Baseline and EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	48	
Units: units on scale				
arithmetic mean (standard deviation)	-10.411 (± 21.8268)	-13.143 (± 28.4467)	-5.953 (± 22.6358)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Skindex-16 Functioning Scale Scores at EOT in the ITT population

End point title	Change from baseline in Skindex-16 Functioning Scale Scores at EOT in the ITT population

End point description:

Skindex-16 questionnaire contains 16 questions related to quality of life in subjects with skin disease. It consists of a short 16-item assessment completed by the subject, with each item rated on a 7-point Likert scale (0=never bothered to 6=always bothered). Responses to the Skindex-16 are categorised into three subscales: symptom, emotional, and functional; and their respective scores are expressed in a linear scale from 0 (no effect) to 100 (effect experienced all the time). Functioning scale score is an average of items 12 to 16.

End point type	Secondary

End point timeframe:

Baseline and EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	51	50	48	
Units: units on scale				
arithmetic mean (standard deviation)	-10.392 (± 23.5294)	-7.267 (± 27.6823)	-0.764 (± 20.1090)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in weekly average of Itch Numeric Rating Scale (NRS) at EOT in the ITT population

End point title	Change from baseline in weekly average of Itch Numeric Rating Scale (NRS) at EOT in the ITT population

End point description:

The Itch NRS is a validated, self-reported, instrument for measurement of itch intensity and subjects were asked to rate the intensity of their itch on an 11-point scale ranging from 0 (no itch) to 10 (worst itch imaginable); higher scores indicated greater itch intensity. The Itch NRS scores were recorded by the subject using the e-diary once daily from screening through the last visit.

End point type	Secondary

End point timeframe:

Baseline and EOT

End point values	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	48	
Units: units on scale				
arithmetic mean (standard deviation)	-1.302 (± 2.8165)	-1.537 (± 3.2634)	-0.547 (± 2.4239)	

Statistical analyses

No statistical analyses for this end point

Secondary: Trough plasma concentrations of JTE-451 in the PK population

End point title	Trough plasma concentrations of JTE-451 in the PK population

End point description:

Trough plasma concentration (measured concentration at the end of a dosing interval at steady state [taken directly before next administration]). Blood samples were collected at specific timepoints to measure trough plasma concentration of JTE-451 in the PK population.

End point type	Secondary

End point timeframe:

Week 0 (pre-dose), Week 4 (pre-dose), Week 8 (pre-dose), Week 12 (pre-dose), and Week 16 (trough)

End point values	JTE-451 200 mg BID - PK Population	JTE-451 400 mg BID - PK Population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	51[9]	50[10]		
Units: nanogram per millilitre (ng/mL)				
arithmetic mean (standard deviation)				
Week 0 (pre-dose)	0 (± 0)	0 (± 0)		
Week 4 (pre-dose)	444 (± 581)	687 (± 602)		
Week 8 (pre-dose)	388 (± 439)	751 (± 1490)		
Week 12 (pre-dose)	355 (± 271)	876 (± 1480)		
Week 16 (trough)	575 (± 704)	1210 (± 1660)		

Notes:

[9] - Analysis set description provides the details for the number of subjects analysed at each timepoint.

[10] - Analysis set description provides the details for the number of subjects analysed at each timepoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs occurring (initial occurrence or a worsening of a pre-existing condition) after the informed consent was signed and up to 4 weeks (28 days) after the last dose of study treatment were reported.

Adverse event reporting additional description:

The treatment-emergent AEs (AEs that occurred during the treatment period or the follow-up period) are presented here for the safety population.

The safety population consisted of the randomised subjects who received at least one dose of the study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	JTE-451 200 mg BID

Reporting group description:

The subjects received a total daily dose of 400 mg of JTE-451.

Reporting group title	JTE-451 400 mg BID

Reporting group description:

The subjects received a total daily dose of 800 mg of JTE-451.

Reporting group title	Placebo

Reporting group description:

The subjects received a placebo-treatment.

Serious adverse events	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 51 (1.96%)	2 / 50 (4.00%)	1 / 50 (2.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 51 (0.00%)	1 / 50 (2.00%)	0 / 50 (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
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Breast abscess			
subjects affected / exposed	1 / 51 (1.96%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 50 (2.00%)	0 / 50 (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

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	JTE-451 200 mg BID	JTE-451 400 mg BID	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 51 (39.22%)	22 / 50 (44.00%)	17 / 50 (34.00%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 51 (1.96%)	3 / 50 (6.00%)	1 / 50 (2.00%)
occurrences (all)	1	3	1
Blood glucose increased			
subjects affected / exposed	2 / 51 (3.92%)	1 / 50 (2.00%)	2 / 50 (4.00%)
occurrences (all)	2	1	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 51 (3.92%)	2 / 50 (4.00%)	0 / 50 (0.00%)
occurrences (all)	2	2	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 51 (3.92%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences (all)	3	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 51 (7.84%)	1 / 50 (2.00%)	2 / 50 (4.00%)
occurrences (all)	8	1	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 51 (3.92%)	2 / 50 (4.00%)	1 / 50 (2.00%)
occurrences (all)	2	2	1

Abdominal pain upper			
subjects affected / exposed	4 / 51 (7.84%)	2 / 50 (4.00%)	0 / 50 (0.00%)
occurrences (all)	4	3	0
Diarrhoea			
subjects affected / exposed	7 / 51 (13.73%)	19 / 50 (38.00%)	3 / 50 (6.00%)
occurrences (all)	13	30	3
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	2 / 50 (4.00%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 51 (1.96%)	2 / 50 (4.00%)	1 / 50 (2.00%)
occurrences (all)	1	4	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 51 (5.88%)	2 / 50 (4.00%)	5 / 50 (10.00%)
occurrences (all)	4	2	5
Pharyngitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 50 (0.00%)	2 / 50 (4.00%)
occurrences (all)	1	0	2
Sinusitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 50 (0.00%)	2 / 50 (4.00%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	2 / 51 (3.92%)	3 / 50 (6.00%)	4 / 50 (8.00%)
occurrences (all)	2	3	4
Urinary tract infection			
subjects affected / exposed	3 / 51 (5.88%)	3 / 50 (6.00%)	0 / 50 (0.00%)
occurrences (all)	4	3	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported