Clinical trial results:
A Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy and Safety of JTE-051 Administered for 12 Weeks to Subjects with Active Rheumatoid Arthritis (MOVE-RA)

Summary

EudraCT number	2015-003140-39
Trial protocol	BG PL
Global end of trial date	25 June 2018

Results information

Result version number	v1 (current)
This version publication date	04 September 2019
First version publication date	04 September 2019

Trial information

Trial identification

Sponsor protocol code	AE051-G-13-003

Additional study identifiers

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

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	18 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 June 2018
Global end of trial reached?	Yes
Global end of trial date	25 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the clinical efficacy of JTE-051 in subjects with active rheumatoid arthritis receiving background non-biologic disease-modifying anti-rheumatic drug therapy
- To evaluate the safety and tolerability of JTE-051 administered for 12 weeks to subjects with active rheumatoid arthritis receiving background non-biologic disease-modifying anti-rheumatic drug therapy
- To evaluate the pharmacokinetics of JTE-051 in plasma of subjects with active rheumatoid arthritis

Protection of trial subjects:

This study was conducted in compliance with the protocol, Good Clinical Practice (GCP) and the applicable regulatory requirement(s) (e.g., 21 CFR Part 50, 56, 312 in the US), Sponsor’s and/or Contract Research Organization (CRO) policies and procedures and all clinical trial regulations. The ICF and other written information provided to subjects were to be revised whenever important new information that may have been relevant to the subject’s consent became available. The revised ICF and other written information were to be approved by the IRB/IEC in advance of use. The subjects were to be informed in a timely manner when new information became available that may have been relevant to their willingness to continue participation in the study. The communication of this information was to be documented. The Investigator, or a person designated by the Investigator, fully informed the subject of all pertinent aspects of the study, including the written information and approval by the IRB/IEC.

Background therapy:

Background treatment with up to two non-biologic DMARDs including methotrexate and one of the following medications (optional): sulfasalazine ≤3 g/day, hydroxychloroquine ≤400 mg/day or chloroquine: ≤250 mg/day, at the time of the Screening Visit. Subjects were to receive up to two non-biologic DMARDs, including methotrexate, at a stable dose and route of administration for at least 12 weeks prior to Visit 2 (Randomization visit) and continue receiving background treatment of up to two non-biologic DMARDs at a stable dose during the study.

Evidence for comparator: -

Actual start date of recruitment	19 September 2016
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: 5
Country: Number of subjects enrolled	Bulgaria: 25
Country: Number of subjects enrolled	Argentina: 20
Country: Number of subjects enrolled	Mexico: 67
Country: Number of subjects enrolled	Peru: 46
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Ukraine: 69

Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	259
EEA total number of subjects	38

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	225
From 65 to 84 years	34
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Written informed consent was obtained prior to performing any study-related procedures. A copy of the informed consent was provided to each subject enrolled in this study. To qualify for the study, subjects were required to satisfy defined criteria.

Pre-assignment

Screening details:

Following signature of the informed consent for the study, screening procedures (up to a 28-day Screening Period) to confirm eligibility were performed across multiple days, as needed, during the Screening Period. A total of 528 subjects were screened, 268 subjects were screen failures and 259 subjects were included in the randomized population.

Period 1

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

Blinding implementation details:

This study was double-blind (i.e., 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). The JTE-051 50 mg tablets, as well as the placebo tablets were supplied as unbranded tablets which are identical in appearance.

Arms

Are arms mutually exclusive?	Yes
Arm title	JTE-051 50 mg

Arm description:

Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 Placebo, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.

Arm type	Experimental
Investigational medicinal product name	JTE-051 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The subjects receive JTE-051 50 mg QD.

Arm title	JTE-051 100 mg

Arm description:

Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.

Arm type	Experimental
Investigational medicinal product name	JTE-051 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

The subjects receive JTE-051 100 mg QD.

Arm title	JTE-051 150 mg

Arm description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 50 mg and JTE-051 Placebo) taken in the morning from the blister card.	
Arm type	Experimental
Investigational medicinal product name	JTE-051 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
The subjects receive JTE-051 150 mg QD.	
Arm title	JTE-051 200 mg
Arm description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 50 mg and JTE-051 50 mg) taken in the morning from the blister card.	
Arm type	Experimental
Investigational medicinal product name	JTE-051 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
The subjects receive JTE-051 200 mg QD.	
Arm title	Placebo
Arm description:	
Each dose consisted of 4 tablets (JTE-051 Placebo, JTE-051 Placebo, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.	
Arm type	Placebo
Investigational medicinal product name	JTE-051 Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
The subjects receive Placebo QD.	

Number of subjects in period 1[1]	JTE-051 50 mg	JTE-051 100 mg	JTE-051 150 mg
Started	51	51	52
Completed	45	43	47
Not completed	6	8	5
Consent withdrawn by subject	2	3	1
Inclusion/exclusion criteria not met	1	1	1
Adverse event, non-fatal	3	3	3
Death	-	1	-
Lost to follow-up	-	-	-

Number of subjects in period 1[1]	JTE-051 200 mg	Placebo
Started	51	52
Completed	38	48
Not completed	13	4
Consent withdrawn by subject	2	2
Inclusion/exclusion criteria not met	1	-
Adverse event, non-fatal	9	2
Death	-	-
Lost to follow-up	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 259 patients were enrolled in the study, 257 patients were included in the Intent-to-treat population.

Baseline characteristics

Reporting groups	
Reporting group title	JTE-051 50 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 Placebo, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.	
Reporting group title	JTE-051 100 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.	
Reporting group title	JTE-051 150 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 50 mg and JTE-051 Placebo) taken in the morning from the blister card.	
Reporting group title	JTE-051 200 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 50 mg and JTE-051 50 mg) taken in the morning from the blister card.	
Reporting group title	Placebo
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 Placebo, JTE-051 Placebo, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.	

Reporting group values	JTE-051 50 mg	JTE-051 100 mg	JTE-051 150 mg
Number of subjects	51	51	52
Age categorical Units: Subjects			
Adults (18-64 years)	42	48	46
From 65-84 years	9	3	6
Age continuous Units: years			
median	52	53	48
full range (min-max)	23 to 74	30 to 69	26 to 72
Gender categorical Units: Subjects			
Female	41	40	44
Male	10	11	8

Reporting group values	JTE-051 200 mg	Placebo	Total
Number of subjects	51	52	257
Age categorical Units: Subjects			
Adults (18-64 years)	43	44	223
From 65-84 years	8	8	34
Age continuous Units: years			
median	51	53	
full range (min-max)	26 to 72	24 to 75	-

Gender categorical Units: Subjects			
Female	43	43	211
Male	8	9	46

Subject analysis sets

Subject analysis set title	Randomized subjects (RAND)
Subject analysis set type	Full analysis

Subject analysis set description:

RAND includes all randomized subjects.

Subject analysis set title	Safety population (SAFE)
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population consists of subjects who were randomly assigned to treatment and who received at least one dose of study drug.

Subject analysis set title	PK Population (PK)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

PK population includes all randomized subjects who received at least one dose of study drug and have at least one usable JTE-051 plasma concentration measurement.

Subject analysis set title	Intent-to-Treat Population (ITT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Intent-to-treat population (ITT) includes all randomized subjects who received at least one dose of study drug and have at least one post-baseline efficacy assessments during the double-blind Treatment Period.

Subject analysis set title	Per Protocol (PP)
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol (PP) is a subset of the ITT population in which subjects did not have any major protocol deviations and met overall 80% to 120% compliance.

Subject analysis set title	JTE-051 analysis set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

JTE-051 analysis set includes all subjects which have been treated with JTE-051.

Reporting group values	Randomized subjects (RAND)	Safety population (SAFE)	PK Population (PK)
Number of subjects	259	258	183
Age categorical Units: Subjects			
Adults (18-64 years)	225		
From 65-84 years	34		
Age continuous Units: years			
median	52	52	
full range (min-max)	23 to 75	23 to 75	
Gender categorical Units: Subjects			
Female	212	211	
Male	47	47	

Reporting group values	Intent-to-Treat Population (ITT)	Per Protocol (PP)	JTE-051 analysis set
Number of subjects	257	206	206
Age categorical Units: Subjects			
Adults (18-64 years)	223		
From 65-84 years	34		
Age continuous Units: years			
median	52	51.5	
full range (min-max)	23 to 75	23 to 73	
Gender categorical Units: Subjects			
Female	211	168	
Male	46	38	

End points

End points reporting groups

Reporting group title	JTE-051 50 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 Placebo, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.	
Reporting group title	JTE-051 100 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.	
Reporting group title	JTE-051 150 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 50 mg and JTE-051 Placebo) taken in the morning from the blister card.	
Reporting group title	JTE-051 200 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 50 mg and JTE-051 50 mg) taken in the morning from the blister card.	
Reporting group title	Placebo
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 Placebo, JTE-051 Placebo, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.	
Subject analysis set title	Randomized subjects (RAND)
Subject analysis set type	Full analysis
Subject analysis set description:	
RAND includes all randomized subjects.	
Subject analysis set title	Safety population (SAFE)
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety population consists of subjects who were randomly assigned to treatment and who received at least one dose of study drug.	
Subject analysis set title	PK Population (PK)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
PK population includes all randomized subjects who received at least one dose of study drug and have at least one usable JTE-051 plasma concentration measurement.	
Subject analysis set title	Intent-to-Treat Population (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intent-to-treat population (ITT) includes all randomized subjects who received at least one dose of study drug and have at least one post-baseline efficacy assessments during the double-blind Treatment Period.	
Subject analysis set title	Per Protocol (PP)
Subject analysis set type	Per protocol
Subject analysis set description:	
Per protocol (PP) is a subset of the ITT population in which subjects did not have any major protocol deviations and met overall 80% to 120% compliance.	
Subject analysis set title	JTE-051 analysis set
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
JTE-051 analysis set includes all subjects which have been treated with JTE-051.	

Primary: ACR20 Response Rate at EOT

End point title	ACR20 Response Rate at EOT[1][2]

End point description:

ACR20 = Percentage of subjects achieving at least 20% improvement from baseline in tender and swollen joint counts and at least 20% improvement in the three of the five remaining American College of Rheumatology core set measures.

End point type	Primary

End point timeframe:

The primary efficacy endpoint was the ACR20 response rate at End of Treatment.

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: Statistical Analysis was performed using the Fisher's exact test at the two-sided 5% significance level.
Result: No statistically significant differences in ACR20 response rate were noted between the placebo group and any of JTE-051 dose group.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: ACR20 Response Rate at EOT has been compared for each treatment arm with Placebo.

End point values	JTE-051 50 mg	JTE-051 100 mg	JTE-051 150 mg	JTE-051 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	52	51
Units: Percent				
number (confidence interval 95%)				
Treatment-Placebo (%)	-3.9 (-23.2 to 15.4)	3.9 (-15.2 to 23.0)	-2.9 (-22.2 to 16.5)	2.0 (-17.2 to 21.1)

Statistical analyses

No statistical analyses for this end point

Primary: JTE-051 Trough Plasma Concentrations

End point title	JTE-051 Trough Plasma Concentrations[3][4]

End point description:

End point type	Primary

End point timeframe:

For Pharmacokinetic Analysis, descriptive statistics of the trough plasma concentration of JTE-051 were presented by treatment at Week 12.

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: For PK data, descriptive statistics of the trough plasma concentration of JTE-051 were presented.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Trough plasma concentration of JTE-051 was measured for subjects who received the active treatment with JTE-051 only. Placebo group is not described here.

End point values	JTE-051 50 mg	JTE-051 100 mg	JTE-051 150 mg	JTE-051 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	42	40	35
Units: ng/mL				
arithmetic mean (standard deviation)				
Concentrations (ng/mL)	119 (± 96.9)	178 (± 156)	312 (± 252)	354 (± 281)

Statistical analyses

No statistical analyses for this end point

Primary: Safety and tolerability of JTE-051

End point title	Safety and tolerability of JTE-051[5]

End point description:

End point type	Primary

End point timeframe:

Evaluation of safety and tolerability of JTE-051 has been administered for 12 weeks to subjects with active rheumatoid arthritis receiving background non-biologic DMARD therapy.

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: Descriptive statistics were presented.

End point values	JTE-051 50 mg	JTE-051 100 mg	JTE-051 150 mg	JTE-051 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	51	52	51
Units: Patients				
Number of subjects with TEAEs	26	21	32	34
Number of subjects with serious TEAEs	2	2	2	1
Number of deaths	0	1	0	0

End point values	Placebo	Safety population (SAFE)	JTE-051 analysis set	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	52	257	206	
Units: Patients				
Number of subjects with TEAEs	22	135	113	
Number of subjects with serious TEAEs	0	7	7	
Number of deaths	0	1	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment-emergent adverse events (TEAEs) included events since the first dose of JTE-051/placebo on Day 1.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	JTE-051 50 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 Placebo, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.	
Reporting group title	JTE-051 100 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.	
Reporting group title	JTE-051 150 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 50 mg and JTE-051 Placebo) taken in the morning from the blister card.	
Reporting group title	JTE-051 200 mg
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 50 mg, JTE-051 50 mg, JTE-051 50 mg and JTE-051 50 mg) taken in the morning from the blister card.	
Reporting group title	Placebo
Reporting group description:	
Each dose consisted of 4 tablets (JTE-051 Placebo, JTE-051 Placebo, JTE-051 Placebo and JTE-051 Placebo) taken in the morning from the blister card.	

Serious adverse events	JTE-051 50 mg	JTE-051 100 mg	JTE-051 150 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 51 (3.92%)	3 / 52 (5.77%)	2 / 52 (3.85%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			

subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	1 / 52 (1.92%)
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			
Appendicitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	0 / 52 (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
Cellulitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 52 (1.92%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Serious adverse events	JTE-051 200 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	

number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 51 (1.96%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rheumatoid arthritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 52 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	JTE-051 50 mg	JTE-051 100 mg	JTE-051 150 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 51 (50.98%)	21 / 52 (40.38%)	32 / 52 (61.54%)
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 51 (3.92%)	1 / 52 (1.92%)	2 / 52 (3.85%)
occurrences (all)	2	1	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 52 (1.92%)	3 / 52 (5.77%)
occurrences (all)	1	1	3
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 51 (5.88%)	1 / 52 (1.92%)	6 / 52 (11.54%)
occurrences (all)	3	1	6
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 51 (3.92%)	1 / 52 (1.92%)	4 / 52 (7.69%)
occurrences (all)	2	1	4
Urinary tract infection			
subjects affected / exposed	3 / 51 (5.88%)	3 / 52 (5.77%)	5 / 52 (9.62%)
occurrences (all)	3	3	5

Non-serious adverse events	JTE-051 200 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 51 (66.67%)	22 / 52 (42.31%)	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	9 / 51 (17.65%)	0 / 52 (0.00%)	
occurrences (all)	9	0	
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	1 / 52 (1.92%) 1	
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	0 / 52 (0.00%) 0	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 52 (0.00%) 0	
Urinary tract infection subjects affected / exposed occurrences (all)	8 / 51 (15.69%) 8	2 / 52 (3.85%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 March 2016	The key changes in Protocol Amendment 1, Version 2 (dated: 24 March 2016) include the following: - The eligibility cut-off for hs-CRP was modified from >1.2 x ULN to ≥1.2 x ULN - Paragraph describing the use of non-hs-CRP as a supportive efficacy parameter was added. - Paragraph describing the currently known joint-related risks associated with NGF inhibitors and the available related information based on the JTE-051 clinical data to date was added. - Exclusion criterion #6: the unit for eGFR was modified from mL/min to mL/min/1.73 m2. - Exclusion criterion #14: note added to state that subjects with confirmed Zika infection within 4 weeks prior to the Screening Visit (Visit 1) are prohibited from participating in the study, whether or not the subjects had received antiviral therapy. - Exclusion criterion #25: this criterion was modified to add known history or suspected (according to the Investigator's judgement) presence of RPOA, spontaneous osteonecrosis of the knee, subchondral insufficiency fractures, Kellgren grade 4 osteoarthritis or pathologic fractures to the list of exclusionary conditions. - Exclusion criterion #26: this was added as a new criterion - Exclusion criterion #34: Sickle cell disease was added as an example of hematological conditions that would exclude the subject from participating in the study. - The following conditions that would mandate removal of subjects from the study were added: total joint replacement procedure, osteonecrosis and RPOA. Additionally, a paragraph was added to state that subjects that develop signs and symptoms consistent with motor polyneuropathy, according to the neurologist's assessment were suspended study drug dosing, pending future assessments. Decision whether the subject may restart study drug was made by the Investigator based on recommendations made by the neurologist. - Isoniazid was added to the list of medications prohibited within 3 months (12 weeks) prior to Day 1 (Visit 2) through Visit 7.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported