Clinical trial results:
A Phase II, Dose Ranging, Exploratory Clinical Study to Assess the Efficacy, Pharmacodynamics, Pharmacokinetics, and Safety of LNP1955 in Patients with Moderate to Severe Rheumatoid Arthritis.

Summary

EudraCT number	2016-001532-35
Trial protocol	HU BG
Global end of trial date	11 October 2017

Results information

Result version number	v1 (current)
This version publication date	07 March 2020
First version publication date	07 March 2020

Trial information

Trial identification

Sponsor protocol code	LRP/LNP1955/2016/002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Lupin Ltd
Sponsor organisation address	46A/47A, Village Nande, Taluka Mulshi, Pune, India, 412115
Public contact	Project Director, Lupin Limited , Lupin Limited, +91 2067917368, chiragshah@lupin.com
Scientific contact	Project Director, Lupin Limited, Lupin Limited, +91 2067917368, chiragshah@lupin.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	11 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 October 2017
Global end of trial reached?	Yes
Global end of trial date	11 October 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

•The primary objective is to assess the proof of efficacy of LNP1955 and find an optimum dose in patients with moderate to severe rheumatoid arthritis (RA).

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki including amendments in force up to and including the time the study was conducted. The study was conducted in compliance with the International Conference on Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP) (Committee for Proprietary Medicinal Products (CPMP) guideline CPMP/ICH/135/95), and compliant with the European Union Clinical Trial Directive (EU CTD): Directive 2001/20/EC.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 October 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: 14
Country: Number of subjects enrolled	Bulgaria: 25
Country: Number of subjects enrolled	Hungary: 19
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	46

From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 80 patients were screened for the study out of which 22 were screen failures and 58 were enrolled into the study. Among those, 48 were randomized in the main double-blind part and 10 patients on methotrexate (MTX) add-on part of the study.

Pre-assignment

Screening details:

A total of 80 patients were screened and 58 were enrolled into the study.

Period 1

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

Blinding implementation details:

The Main part of the study was a randomized, double-blind, comparative, placebo-controlled, parallel-group. The MTX Add-on part was an open-label study. Based on ongoing safety monitoring & laboratory data, considerable number of patients from treated arms were observed to have elevations in Aspartate Aminotransferase (AST)/ Alanine Aminotransferase (ALT) of >3 times normal. Therefore, in view of patients' safety, unblinding of these was done by Sponsor.

Arms

Are arms mutually exclusive?	Yes
Arm title	Main Part: Placebo

Arm description:

Twice daily (bid) dose of Matching placebo was administered orally.

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

Dosage and administration details:

Matching placebo was administered twice daily (bid) orally for 12 weeks.

Arm title	Main Part: LNP1955 (40 mg)

Arm description:

Twice daily (bid) dose of LNP1955 (40 mg) was administered orally.

Arm type	Experimental
Investigational medicinal product name	LNP1955
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

40 mg of LNP 1955 was administered twice daily (bid) orally for 12 weeks.

Arm title	Main Part: LNP1955 (80 mg)

Arm description:

Twice daily (bid) dose of LNP1955 (80 mg) was administered orally.

Arm type	Experimental

Investigational medicinal product name	LNP1955
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

80 mg of LNP1955 was administered twice daily (bid) orally for 12 weeks.

Arm title	MTX Add-on part

Arm description:

Twice daily (bid) dose of LNP1955 (40 mg) was administered orally. and a dose of 7.5 mg of methotrexate was administered orally (in 3 divided doses of 2.5 mg, approximately 12 hours apart) in a week.

Arm type	Experimental
Investigational medicinal product name	LNP1955
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

40 mg of LNP 1955 was administered twice daily (bid) orally for 12 weeks.

Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A dose of 2.5 mg of methotrexate was administered orally once in a week for 12 weeks.

Number of subjects in period 1	Main Part: Placebo	Main Part: LNP1955 (40 mg)	Main Part: LNP1955 (80 mg)
Started	16	16	16
Completed	9	8	7
Not completed	7	8	9
Consent withdrawn by subject	-	2	2
Physician decision	-	-	2
Adverse event, non-fatal	1	3	1
Sponsor decision	6	3	4

Number of subjects in period 1	MTX Add-on part
Started	10
Completed	8
Not completed	2
Consent withdrawn by subject	-
Physician decision	1
Adverse event, non-fatal	-
Sponsor decision	1

Baseline characteristics

Reporting groups	
Reporting group title	Main Part: Placebo
Reporting group description:	
Twice daily (bid) dose of Matching placebo was administered orally.	
Reporting group title	Main Part: LNP1955 (40 mg)
Reporting group description:	
Twice daily (bid) dose of LNP1955 (40 mg) was administered orally.	
Reporting group title	Main Part: LNP1955 (80 mg)
Reporting group description:	
Twice daily (bid) dose of LNP1955 (80 mg) was administered orally.	
Reporting group title	MTX Add-on part
Reporting group description:	
Twice daily (bid) dose of LNP1955 (40 mg) was administered orally. and a dose of 7.5 mg of methotrexate was administered orally (in 3 divided doses of 2.5 mg, approximately 12 hours apart) in a week.	

Reporting group values	Main Part: Placebo	Main Part: LNP1955 (40 mg)	Main Part: LNP1955 (80 mg)
Number of subjects	16	16	16
Age categorical Units: Subjects			
Adults (18-64 years)	12	13	11
From 65-84 years	4	3	5
Gender categorical Units: Subjects			
Female	12	12	13
Male	4	4	3

Reporting group values	MTX Add-on part	Total	
Number of subjects	10	58	
Age categorical Units: Subjects			
Adults (18-64 years)	10	46	
From 65-84 years	0	12	
Gender categorical Units: Subjects			
Female	9	46	
Male	1	12	

End points

End points reporting groups

Reporting group title	Main Part: Placebo
Reporting group description:	
Twice daily (bid) dose of Matching placebo was administered orally.	
Reporting group title	Main Part: LNP1955 (40 mg)
Reporting group description:	
Twice daily (bid) dose of LNP1955 (40 mg) was administered orally.	
Reporting group title	Main Part: LNP1955 (80 mg)
Reporting group description:	
Twice daily (bid) dose of LNP1955 (80 mg) was administered orally.	
Reporting group title	MTX Add-on part
Reporting group description:	
Twice daily (bid) dose of LNP1955 (40 mg) was administered orally. and a dose of 7.5 mg of methotrexate was administered orally (in 3 divided doses of 2.5 mg, approximately 12 hours apart) in a week.	

Primary: Proportion of patients achieving an American College of Rheumatology 20% (ACR20) response at Week 12.

End point title	Proportion of patients achieving an American College of Rheumatology 20% (ACR20) response at Week 12.[1]
End point description:	
Efficacy & PD was not analyzed, as the study was terminated by the sponsor due to safety reasons	
End point type	Primary
End point timeframe:	
American College of Rheumatology 20% (ACR20) response at Week 12.	

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: Based on ongoing safety monitoring of study, considerable number of patients reported elevations in AST/ALT in active treatment arms, thus indicating an unfavorable risk: benefit ratio. Such a potential risk for liver enzyme elevation is undesirable. In light of this cumulative assessment and keeping patient safety in mind, Sponsor decided to prematurely terminate the study and hence efficacy analysis (primary and secondary), PK-PD analysis was not performed.

End point values	Main Part: Placebo	Main Part: LNP1955 (40 mg)	Main Part: LNP1955 (80 mg)	MTX Add-on part
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: Numbers				

Notes:

[2] - No Efficacy analysis done for this study

[3] - No Efficacy analysis done for this study

[4] - No Efficacy analysis done for this study

[5] - No Efficacy analysis done for this study

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs), vital signs, Physical examination were evaluated up to 12 weeks of treatment and follow-up period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Main Part: Placebo

Reporting group description:

Twice daily (bid) dose of Matching placebo was administered orally.

Reporting group title	Main Part: LNP1955 (40 mg)

Reporting group description:

Twice daily (bid) dose of LNP1955 (40 mg) was administered orally.

Reporting group title	Main Part: LNP1955 (80 mg)

Reporting group description:

Twice daily (bid) dose of LNP1955 (80 mg) was administered orally.

Reporting group title	MTX Add-on part

Reporting group description:

Twice daily (bid) dose of LNP1955 (40 mg) was administered orally. and a dose of 7.5 mg of methotrexate was administered orally (in 3 divided doses of 2.5 mg, approximately 12 hours apart) in a week.

Serious adverse events	Main Part: Placebo	Main Part: LNP1955 (40 mg)	Main Part: LNP1955 (80 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 16 (12.50%)	0 / 16 (0.00%)	1 / 16 (6.25%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (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

Serious adverse events	MTX Add-on part		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Main Part: Placebo	Main Part: LNP1955 (40 mg)	Main Part: LNP1955 (80 mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 16 (31.25%)	11 / 16 (68.75%)	9 / 16 (56.25%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 16 (0.00%)	3 / 16 (18.75%)	0 / 16 (0.00%)
occurrences (all)	0	4	0
Arteriosclerosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			

subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Persistent depressive disorder			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Investigations			
Neutrophil count increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	2 / 16 (12.50%)	4 / 16 (25.00%)
occurrences (all)	0	2	4
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	4 / 16 (25.00%)
occurrences (all)	0	1	4
Blood cholesterol increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Monocyte count decreased			

subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Blood glucose increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Transaminases increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Cardiomegaly			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eosinophilia			

subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Swelling of eyelid			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Flatulence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Aphthous ulcer			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Chronic gastritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cholelithiasis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Folliculitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Laryngitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Ascariasis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Herpes virus infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Bronchitis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Septic shock			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	MTX Add-on part		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 10 (50.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	0		
Arteriosclerosis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Haemorrhoids			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Persistent depressive disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Investigations			
Neutrophil count increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Blood cholesterol increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Monocyte count decreased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood glucose increased			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Transaminases increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Cardiomegaly			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Microcytic anaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Lymphopenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Eosinophilia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eye disorders			
Swelling of eyelid			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Flatulence subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Gastritis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Aphthous ulcer subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Chronic gastritis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Hepatobiliary disorders			
Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Cholelithiasis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Urticaria subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Pruritus			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Alopecia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Folliculitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Laryngitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ascariasis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Herpes virus infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Septic shock			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pneumonia			

subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all) Hypertriglyceridaemia subjects affected / exposed occurrences (all)	 1 / 10 (10.00%) 1 1 / 10 (10.00%) 1		

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

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

Based on ongoing safety monitoring considerable number of patients reported elevations in AST/ALT in active treatments arms hence, study was terminated prematurely in view of patient's safety.

Notes: