Clinical trial results:
A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study to Evaluate the Safety, Pharmacokinetics, and Efficacy of VX-509 using Magnetic Resonance Imaging and Arthroscopic Biopsies in Subjects with Active Rheumatoid Arthritis on Stable Disease-Modifying Antirheumatic Drugs

Summary

EudraCT number	2012-003439-41
Trial protocol	LT EE DK NL
Global end of trial date	09 January 2014

Results information

Result version number	v1 (current)
This version publication date	28 June 2016
First version publication date	07 August 2015

Trial information

Trial identification

Sponsor protocol code	VX12-509-103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01754935
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vertex Pharmaceuticals Incorporated
Sponsor organisation address	50 Northern Avenue, Boston, MA, United States, 02210-1862
Public contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 617-341-6777, medicalinfo@vrtx.com
Scientific contact	Medical Monitor, Vertex Pharmaceuticals Incorporated, 1 617-341-6777, medicalinfo@vrtx.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	25 April 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

During 12 weeks of treatment in subjects with active rheumatoid arthritis (RA) on stable disease-modifying antirheumatic drug (DMARD) therapy: to evaluate the efficacy of VX-509 across a range of doses and to evaluate the early effect of VX-509 administration on joint structures as assessed by magnetic resonance imaging (MRI).

Protection of trial subjects:

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP).

Background therapy:

Stable treatment with 1 of the following DMARDs: methotrexate, sulfasalazine, leflunomide, penicillamine, or antimalarial drug.

Evidence for comparator:

No active comparator.

Actual start date of recruitment	17 December 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Estonia: 2
Country: Number of subjects enrolled	United States: 38
Country: Number of subjects enrolled	Lithuania: 3
Worldwide total number of subjects	43
EEA total number of subjects	5

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)	40
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All 43 subjects were included in the Safety Set, and all 38 randomized subjects were included in the Full Analysis Set (FAS).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received 6 VX-509-matched placebo tablets orally once daily for 12 weeks.

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:

6 VX-509-matched placebo tablets orally once daily for 12 weeks.

Arm title	VX-509 100 mg

Arm description:

Subjects received 2 VX-509 50 milligram (mg) tablets and 4 VX-509-matched placebo tablets orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	VX-509
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 VX-509 50 mg tablets and 4 VX-509-matched placebo tablets orally once daily for 12 weeks.

Arm title	VX-509 200 mg

Arm description:

Subjects received 4 VX-509 50 mg tablets and 2 VX-509-matched placebo tablets orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	VX-509
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
4 VX-509 50 mg tablets and 2 VX-509-matched placebo tablets orally once daily for 12 weeks.

Arm title	VX-509 300 mg

Arm description:
Subjects received 6 VX-509 50 mg tablets orally once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	VX-509
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
6 VX-509 50 mg tablets orally once daily for 12 weeks.

Number of subjects in period 1	Placebo	VX-509 100 mg	VX-509 200 mg
Started	12	11	10
Completed	11	10	10
Not completed	1	1	0
Consent withdrawn by subject	1	-	-
Lost to follow-up	-	1	-

Number of subjects in period 1	VX-509 300 mg
Started	10
Completed	10
Not completed	0
Consent withdrawn by subject	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received 6 VX-509-matched placebo tablets orally once daily for 12 weeks.	
Reporting group title	VX-509 100 mg
Reporting group description:	
Subjects received 2 VX-509 50 milligram (mg) tablets and 4 VX-509-matched placebo tablets orally once daily for 12 weeks.	
Reporting group title	VX-509 200 mg
Reporting group description:	
Subjects received 4 VX-509 50 mg tablets and 2 VX-509-matched placebo tablets orally once daily for 12 weeks.	
Reporting group title	VX-509 300 mg
Reporting group description:	
Subjects received 6 VX-509 50 mg tablets orally once daily for 12 weeks.	

Reporting group values	Placebo	VX-509 100 mg	VX-509 200 mg
Number of subjects	12	11	10
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 52.8 ± 12.25	 56.7 ± 6.47	 50.5 ± 11.9
Gender categorical Units: Subjects			
Female	10	8	5
Male	2	3	5

Reporting group values	VX-509 300 mg	Total	
Number of subjects	10	43	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 54.9 ± 5.04	 -	
Gender categorical Units: Subjects			
Female	8	31	
Male	2	12	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received 6 VX-509-matched placebo tablets orally once daily for 12 weeks.	
Reporting group title	VX-509 100 mg
Reporting group description:	
Subjects received 2 VX-509 50 milligram (mg) tablets and 4 VX-509-matched placebo tablets orally once daily for 12 weeks.	
Reporting group title	VX-509 200 mg
Reporting group description:	
Subjects received 4 VX-509 50 mg tablets and 2 VX-509-matched placebo tablets orally once daily for 12 weeks.	
Reporting group title	VX-509 300 mg
Reporting group description:	
Subjects received 6 VX-509 50 mg tablets orally once daily for 12 weeks.	

Primary: Percentage of Subjects Achieving American College of Rheumatology 20% (ACR20) C-Reactive Protein (ACR20-CRP) Response at Week 12

End point title	Percentage of Subjects Achieving American College of Rheumatology 20% (ACR20) C-Reactive Protein (ACR20-CRP) Response at Week 12
End point description:	
ACR20-CRP response: greater than equal (>=) 20% improvement in tender joints count (TJC); >= 20% improvement in swollen joints count (SJC); and >= 20% improvement in at least 3 of 5 remaining ACR core measures: subject assessment of pain (assessed on 0-100 mm VAS, higher score = more pain); subject global assessment of disease activity (assessed on 0-10 point scale, higher score = more disease activity); physician global assessment of disease activity (assessed on 0-10 point scale, higher score = more disease activity); self-assessed disability (disability index of the Health Assessment Questionnaire [HAQ]); and CRP levels. Analysis was performed on FAS defined as all randomized subjects who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	5	10
Units: percentage of subjects				
number (not applicable)	25	63.6	80	60

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	VX-509 100 mg v Placebo

Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0678
Method	Miettinen-Nurminen method
Parameter estimate	Proportion difference
Point estimate	38.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	68.8

Statistical analysis title	Statistical Analysis 2
Comparison groups	VX-509 200 mg v Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0417
Method	Miettinen-Nurminen method
Parameter estimate	Proportion difference
Point estimate	55
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	82.8

Statistical analysis title	Statistical Analysis 3
Comparison groups	VX-509 300 mg v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1043
Method	Miettinen-Nurminen method
Parameter estimate	Proportion difference
Point estimate	35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.2
upper limit	66.6

Primary: Change From Baseline in Disease Activity Score Using 28-Joint Count and

C-Reactive Protein (4 Variables) (DAS28-4 [CRP]) at Week 12

End point title	Change From Baseline in Disease Activity Score Using 28-Joint Count and C-Reactive Protein (4 Variables) (DAS28-4 [CRP]) at Week 12

End point description:

DAS28-4 (CRP) was calculated from SJC and TJC using the 28 joints count, CRP [mg/L] and subject general health visual analogue scale score. A score of less than (<) 2.6 implied remission and <=3.2 implied low disease activity. Analysis was performed on FAS.

End point type	Primary

End point timeframe:

Baseline, Week 12

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	5	10
Units: units on scale				
least squares mean (standard error)	-0.82 (± 0.419)	-1.41 (± 0.456)	-2.07 (± 0.541)	-2.25 (± 0.421)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The mixed effect model for repeated measures was applied. The model includes the change from baseline of DAS28-4 (CRP) as the dependent variable, treatment group, visit, treatment by visit interaction as fixed effects, and subject as a random effect, with adjustment for the continuous baseline DAS28-4 (CRP), prior use of anti-TNF, and region.

Comparison groups	VX-509 100 mg v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2485
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.62
upper limit	0.42

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Analysis was performed as described in Statistical Analysis 1.

Comparison groups	VX-509 200 mg v Placebo

Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0408
Method	Mixed model effect
Parameter estimate	LS Mean Difference
Point estimate	-1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.46
upper limit	-0.05

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Analysis was performed as described in Statistical Analysis 1.	
Comparison groups	VX-509 300 mg v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0055
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	-1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.44
upper limit	-0.43

Primary: Change from Baseline in Outcome Measures in Rheumatology Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Imaging Scoring System (RAMRIS) Synovitis Score at Week 12

End point title	Change from Baseline in Outcome Measures in Rheumatology Clinical Trials (OMERACT) Rheumatoid Arthritis Magnetic Resonance Imaging Scoring System (RAMRIS) Synovitis Score at Week 12
End point description:	
Synovitis score: individual score 0-3, range 0-27 without interphalangeal (IP) joints. Wrist (4 joints) and metacarpophalangeal (MCP) joints (5 joints) were included in the calculation (IP joints were not included in the calculation). Minimum required number of evaluable joints were 3 for each segment (wrist and MCP joints). Segment scores are the sum of the joints within that segment. RAMRIS synovitis score is calculated as sum of the segment scores. Analysis was performed on FAS.	
End point type	Primary
End point timeframe:	
Baseline, Week 12	

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	5	10
Units: units on scale				
least squares mean (standard error)	-0.44 (± 1.445)	-4.76 (± 1.467)	-5.76 (± 1.66)	-7.68 (± 1.528)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The mixed effect model for repeated measures was applied. The model includes the change from baseline of each scale score of RAMRIS as the dependent variable, treatment group, visit, treatment by visit interaction as fixed effects and subject as a random effect, with adjustment for the continuous baseline, prior use of anti-TNF and region.

Comparison groups	VX-509 100 mg v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0095
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	-4.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	-1.15

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Analysis was performed as described in Statistical Analysis 1.

Comparison groups	VX-509 200 mg v Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0088
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	-5.32

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.18
upper limit	-1.46

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Analysis was performed as described in Statistical Analysis 1.	
Comparison groups	VX-509 300 mg v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	-7.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.66
upper limit	-3.82

Primary: Change from Baseline in OMERACT RAMRIS Osteitis Score at Week 12

End point title	Change from Baseline in OMERACT RAMRIS Osteitis Score at Week 12

End point description:

Osteitis (bone marrow edema) score: individual score 0-3, range 0-75 without IP joints. Wrist (15 joints) and MCP bones (10 joints) were included in the calculation (IP joints were not included in the calculation). Minimum required number of evaluable joints were 8 and 6 for wrist and MCP segment, respectively. Segment scores are the sum of the joints within that segment. RAMRIS synovitis score is calculated as sum of the segment scores. Analysis was performed on FAS.

End point type	Primary

End point timeframe:

Baseline, Week 12

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	5	10
Units: units on scale				
least squares mean (standard error)	-2.91 (± 1.478)	-4.71 (± 1.613)	-5.14 (± 1.765)	-7.41 (± 1.482)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The mixed effect model for repeated measures was applied. The model includes the change from baseline of each scale score of RAMRIS as the dependent variable, treatment group, visit, treatment by visit interaction as fixed effects and subject as a random effect, with adjustment for the continuous baseline, prior use of anti-TNF and region.

Comparison groups	VX-509 100 mg v Placebo
Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2193
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	-1.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.77
upper limit	1.16

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Analysis was performed as described in Statistical Analysis 1.

Comparison groups	VX-509 200 mg v Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.213
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	-2.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.84
upper limit	1.38

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:	
Analysis was performed as described in Statistical Analysis 1.	
Comparison groups	VX-509 300 mg v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0076
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	-4.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.68
upper limit	-1.33

Primary: Change from Baseline in OMERACT RAMRIS Erosion Score at Week 12

End point title	Change from Baseline in OMERACT RAMRIS Erosion Score at Week 12

End point description:

Erosion score: individual score 0-10, range 0-250 without IP joints. Wrist (15 joints) and MCP bones (10 joints) were included in the calculation (IP joints were not included in the calculation). Minimum required number of evaluable joints were 8 and 6 for wrist and MCP segment, respectively. Segment scores are the sum of the joints within that segment. RAMRIS synovitis score is calculated as sum of the segment scores. Analysis was performed on FAS.

End point type	Primary

End point timeframe:

Baseline, Week 12

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	5	10
Units: units on scale				
least squares mean (standard error)	0.15 (± 0.177)	0.45 (± 0.188)	0.37 (± 0.212)	0.35 (± 0.191)

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The mixed effect model for repeated measures was applied. The model includes the change from baseline of each scale score of RAMRIS as the dependent variable, treatment group, visit, treatment by visit interaction as fixed effects and subject as a random effect, with adjustment for the continuous baseline, prior use of anti-TNF and region.

Comparison groups	Placebo v VX-509 100 mg

Number of subjects included in analysis	23
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1274
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.7

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Analysis was performed as described in Statistical Analysis 1.	
Comparison groups	VX-509 200 mg v Placebo
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3587
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.71

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Analysis was performed as described in Statistical Analysis 1.	
Comparison groups	VX-509 300 mg v Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3268
Method	Mixed effect model
Parameter estimate	LS Mean Difference
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.63

Secondary: Percentage of Subjects Achieving ACR50-CRP and ACR70-CRP Response at Week 12

End point title	Percentage of Subjects Achieving ACR50-CRP and ACR70-CRP Response at Week 12

End point description:

ACR50-CRP/ACR70-CRP response: >= 50%/70% improvement in TJC; >= 50%/70% improvement in SJC; and >= 50%/70% improvement in at least 3 of 5 remaining ACR core measures: subject assessment of pain (assessed on 0-100 mm VAS, higher score = more pain); subject global assessment of disease activity (assessed on 0-10 point scale, higher score = more disease activity); physician global assessment of disease activity (assessed on 0-10 point scale, higher score = more disease activity); self-assessed disability (disability index of the HAQ); and CRP levels. Analysis was performed on safety set defined as all subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	10	10
Units: percentage of subjects				
number (not applicable)				
ACR50-CRP Response	8.3	27.3	30	60
ACR70-CRP Response	8.3	18.2	10	20

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with DAS28-4 (CRP) Remission, DAS28-4 (ESR) Remission, and European League Against Rheumatism (EULAR) Moderate or Good Response at Week 12

End point title	Percentage of Subjects with DAS28-4 (CRP) Remission, DAS28-4 (ESR) Remission, and European League Against Rheumatism (EULAR) Moderate or Good Response at Week 12

End point description:

DAS28-4 (CRP) is defined in second primary endpoint. DAS28-4 (CRP) and DAS28-4 (ESR) remission was defined as having a score <2.6. EULAR response criteria were used to measure individual response as none, good, and moderate, depending on the extent of change from baseline and the level of disease activity reached. Good responders: change from baseline >1.2 with DAS28-4 (CRP) =< 3.2; moderate responders: change from baseline >1.2 with DAS28-4 (CRP) >3.2 or change from baseline >0.6 to =<1.2 with DAS28-4 (CRP) =<5.1; non-responders: change from baseline =< 0.6 or change from baseline >0.6 and =<1.2 with DAS28-4 (CRP) >5.1. DAS28-4 (CRP) remission was defined as having a score <2.6.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	10	10
Units: percentage of subjects				
number (not applicable)				
DAS28-4 (CRP) Remission	0	27.3	10	10
DAS28-4 (ESR) Remission	0	9.1	20	30
EULAR Moderate/Good Response	41.7	54.5	60	60

Statistical analyses

No statistical analyses for this end point

Secondary: ACR Hybrid Score at Week 12

End point title	ACR Hybrid Score at Week 12

End point description:

Evaluates the improvement in active RA by combining elements of the ACR20/50/70 with a continuous score of the mean change in core set measures. Analysis was performed on safety set.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	10	10
Units: units on a scale				
least squares mean (standard error)	10.83 (± 9.227)	38.87 (± 10.007)	38.81 (± 9.672)	50.5 (± 9.236)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Health Assessment Questionnaire -Disability Index (HAQ-DI) at Week 12

End point title	Change from baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) at Week 12

End point description:

HAQ-DI is a self-completed subject questionnaire specific for RA. It consists of 20 questions referring to 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and common daily

activities. Each domain has at least 2 component questions. There are 4 possible responses for each component: 0=without any difficulty; 1=with some difficulty; 2=with much difficulty; 3=unable to do. Domain score = total score of individual questions divided by total number of questions. HAQ-DI total score = total of domain scores divided by number of domains, range: 0 (best) to 3 (worst). Analysis was performed on safety set.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	10	10
Units: units on scale				
least squares mean (standard error)	-0.12 (± 0.155)	-0.32 (± 0.168)	-0.47 (± 0.163)	-0.67 (± 0.156)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Physical Function Subscale and Physical and Mental Health Components of the SF-36 at Week 12

End point title	Change from Baseline in the Physical Function Subscale and Physical and Mental Health Components of the SF-36 at Week 12

End point description:

The SF-36 is a general health status questionnaire that assesses 8 domains of functional health and well-being: Physical Functioning, Role Limitations due to Physical Health Problems, Bodily Pain, Social Functioning, Mental Health, Role Limitations due to Emotional Problems, Vitality, and General Health Perceptions. The score for a section is an average of the individual question scores, which are scaled 0-100 (100=highest level of functioning). Change from baseline for physical function subscale is reported. Analysis was performed on safety set.

End point type	Secondary

End point timeframe:

Baseline, Week 12

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	8	9
Units: units on scale				
arithmetic mean (standard deviation)				
Change at Week 12 in Physical Functioning Score	1.216 (± 5.3627)	3.636 (± 6.0822)	7.655 (± 8.9187)	7.754 (± 6.6217)
Change at Week 12 in Mental Component Score	5.111 (± 7.082)	0.737 (± 7.03)	1.645 (± 15.3951)	1.772 (± 10.5995)
Change at Week 12 in Physical Component Score	0.243 (± 6.3369)	7.867 (± 8.2593)	8.694 (± 8.9138)	9.674 (± 7.8496)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in OMERACT RAMRIS Synovitis, Osteitis and Erosion Scores at Week 6

End point title	Change from Baseline in OMERACT RAMRIS Synovitis, Osteitis and Erosion Scores at Week 6

End point description:

Different OMERACT RAMRIS scores are defined in Primary Endpoints. Analysis was performed on safety set.

End point type	Secondary

End point timeframe:

Baseline, Week 6

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	10	10
Units: units on scale				
least squares mean (standard error)				
Change at Week 6 in Synovitis Score	-0.81 (± 1.301)	-3.23 (± 1.382)	-3.26 (± 1.3)	-5.56 (± 1.332)
Change at Week 6 in Osteitis Score	-3.8 (± 1.509)	-4.29 (± 1.655)	-5.17 (± 1.611)	-5.62 (± 1.441)
Change at Week 6 in Erosion Score	0.21 (± 0.163)	0.27 (± 0.177)	0.43 (± 0.165)	0.4 (± 0.17)

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameters of VX -509 and its Metabolite in Plasma: Maximum Observed Concentration [Cmax] at Week 12

End point title	PK parameters of VX -509 and its Metabolite in Plasma: Maximum Observed Concentration [Cmax] at Week 12

End point description:

As per Sponsor’s decision to modify the drug development plan for VX-509, the PK and PK/PD analyses were not performed, hence no data could be reported.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[1]	0[2]	0[3]	0[4]
Units: ng/ml				
number (not applicable)				

Notes:

[1] - Reason for no analysis is provided in endpoint description.

[2] - Reason for no analysis is provided in endpoint description.

[3] - Reason for no analysis is provided in endpoint description.

[4] - Reason for no analysis is provided in endpoint description.

Statistical analyses

No statistical analyses for this end point

Secondary: PK parameters of VX-509 and its Metabolite in Area Under The Concentration Versus Time Curve [AUC] at Week 12

End point title	PK parameters of VX-509 and its Metabolite in Area Under The Concentration Versus Time Curve [AUC] at Week 12

End point description:

As per Sponsor’s decision to modify the drug development plan for VX-509, the PK and PK/PD analyses were not performed, hence no data could be reported.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[5]	0[6]	0[7]	0[8]
Units: ng/mL				
number (not applicable)				

Notes:

[5] - Reason for no analysis is provided in endpoint description.

[6] - Reason for no analysis is provided in endpoint description.

[7] - Reason for no analysis is provided in endpoint description.

[8] - Reason for no analysis is provided in endpoint description.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

AE: any untoward medical occurrence in a subject during the study; the event does not necessarily have a causal relationship with the treatment. This includes any newly occurring event or previous condition that has increased in severity or frequency after the informed consent form is signed. AE included serious as well as non-serious AEs. SAE (subset of AE): medical event or condition, which falls into any of the following categories, regardless of its relationship to the study drug: death, life threatening adverse experience, in-patient hospitalization/prolongation of hospitalization, persistent/significant disability or incapacity, congenital anomaly/birth defect, important medical event. Analysis was performed on safety set included all subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Up to Week 16

End point values	Placebo	VX-509 100 mg	VX-509 200 mg	VX-509 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	11	10	10
Units: percentage of subjects				
number (not applicable)				
Subjects with AEs	41.7	72.7	80	90
Subjects with SAEs	0	9.1	10	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to Week 16	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1
Reporting groups	
Reporting group title	VX-509 100 mg
Reporting group description: VX-509 100 mg tablet orally once daily for 12 weeks.	
Reporting group title	Placebo
Reporting group description: Placebo matched to VX-509 tablet orally once daily for 12 weeks.	
Reporting group title	VX-509 300 mg
Reporting group description: VX-509 300 mg tablet orally once daily for 12 weeks.	
Reporting group title	VX-509 200 mg
Reporting group description: VX-509 200 mg tablet orally once daily for 12 weeks.	

Serious adverse events	VX-509 100 mg	Placebo	VX-509 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Partial seizures			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (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
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (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

Serious adverse events	VX-509 200 mg		
Total subjects affected by serious			

adverse events			
subjects affected / exposed	1 / 10 (10.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Partial seizures			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	VX-509 100 mg	Placebo	VX-509 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 11 (63.64%)	5 / 12 (41.67%)	9 / 10 (90.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Genital rash			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Prostatomegaly			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Sinus congestion			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood erythropoietin increased			
subjects affected / exposed	2 / 11 (18.18%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood triglycerides increased			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural			

complications			
Contusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 11 (0.00%)	2 / 12 (16.67%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Conjunctivitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dry mouth			

subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Lip ulceration			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	1 / 10 (10.00%)
occurrences (all)	1	1	2
Rash papular			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Swelling face			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			

Joint effusion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 11 (9.09%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blister infected			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Body tinea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Herpes virus infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 11 (9.09%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Hyperlipidaemia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	VX-509 200 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 10 (80.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Genital rash			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pelvic pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Prostatomegaly			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Sinus congestion			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Oropharyngeal pain			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Investigations			
Blood erythropoietin increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood triglycerides increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lip ulceration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			

Rash subjects affected / exposed occurrences (all) Rash papular subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Swelling face subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Musculoskeletal and connective tissue disorders Joint effusion subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis	0 / 10 (0.00%) 0		

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Blister infected			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Body tinea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Herpes virus infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hyperlipidaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 September 2012	Updated inclusion exclusion criteria.
09 October 2012	Added secondary endpoint: Change from baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) at Week 12. Updated inclusion criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported