ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 02/27/2014

ClinicalTrials.gov ID: NCT01197521

Study Identification

Unique Protocol ID:	D4300C00001
Brief Title:	Evaluation of Effectiveness of Two Dosing Regimens of Fostamatinib Compared to Placebo in Patients With Rheumatoid Arthritis (RA) Who Are Taking Methotrexate But Not Responding. (OSKIRA - 1)
Official Title:	(OSKIRA-1): A Phase III, Multi-centre, Randomised, Double-Blind, Placebo-Controlled, Parallel Group Study of Two Dosing Regimens of Fostamatinib Disodium in Rheumatoid Arthritis Patients With an Inadequate Response to Methotrexate
Secondary IDs:	2010-020743-12 [EudraCT Number]

Study Status

Record Verification:	February 2014
Overall Status:	Completed
Study Start:	September 2010
Primary Completion:	November 2012 [Actual]
Study Completion:	November 2012 [Actual]

Sponsor/Collaborators

Sponsor:	AstraZeneca
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? Yes Delayed Posting? No
IND/IDE Protocol?:	Yes
IND/IDE Information:	Grantor: CDER IND/IDE Number: 69197 Serial Number: Has Expanded Access? No
Review Board:	Approval Status: Board Name: Board Affiliation: Phone: Email:
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	United States: Food and Drug Administration Belgium: Federal Agency for Medicinal Products and Health Products Bulgaria: Bulgarian Drug Agency Estonia: The State Agency of Medicine France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis) Hungary: National Institute of Pharmacy Poland: Office for Registration of Medicinal Products, Medical Devices and Biocidal Products Slovakia: State Institute for Drug Control Spain: Agencia Española de Medicamentos y Productos Sanitarios Ukraine: Ministry of Health United Kingdom: Medicines and Healthcare Products Regulatory Agency Australia: Department of Health and Ageing Therapeutic Goods Administration India: Drugs Controller General of India Argentina: National Administration of Drugs, Food & Medical Technology (ANMAT) Brazil: National Health Surveillance Agency Chile: Instituto de Salud Pública de Chile Mexico: Federal Commission for Sanitary Risks Protection Peru: General Directorate of Pharmaceuticals, Devices, and Drugs

Study Description

Brief Summary:	The purpose of the study is to evaluate the effectiveness of two dosing regimens of fostamatinib compared to placebo, in patients with rheumatoid arthritis (RA) who are taking methotrexate but not responding. The study will last for 1 year.
Detailed Description:	Sub-study: Full title: Optional Genetic Research

Date: 18 June 2010

Version: 1

Objectives: To collect and store, with appropriate consent ,DNA samples for future exploratory research into genes/genetic variation that may influence response (ie, absorption, distribution, metabolism and excretion, safety, tolerability and efficacy) to fostamatinib disodium and/or methotrexate; and/or susceptibility to, progression of and prognosis of RA

Conditions

Conditions: Rheumatoid Arthritis

Keywords: Rheumatoid Arthritis

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: Phase 3

Intervention Model: Parallel Assignment

Number of Arms: 3

Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)

Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 923 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Dosing Regimen A Oral Treatment	Drug: fostamatinib fostamatinib 100 mg twice daily
Experimental: Dosing Regimen B Oral Treatment	Drug: fostamatinib fostamatinib 100 mg twice daily/150 mg once daily
Placebo Comparator: Dosing Regimen C Oral Treatment	Drug: placebo, fostamatinib Placebo for 24 weeks followed by fostamatinib 100 mg twice daily

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Active rheumatoid arthritis (RA) diagnosed after the age of 16
- Currently taking methotrexate
- 6 or more swollen joints and 6 or more tender/painful joints (from 28 joint count) and either Erythrocyte Sedimentation Rate (ESR) blood result of 28mm/h or more, or C-Reactive Protein (CRP) blood result of 10mg/L or more
- At least one of the following: documented history of positive rheumatoid factor (blood test), current presence of rheumatoid factor (blood test), radiographic erosion within 12 months prior to study enrolment, presence of serum anti-cyclic citrullinated peptide antibodies (blood test)

Exclusion Criteria:

- Females who are pregnant or breast feeding
- Poorly controlled hypertension
- Liver disease or significant liver function test abnormalities
- Certain inflammatory conditions (other than rheumatoid arthritis), connective tissue diseases or chronic pain disorders
- Recent or significant cardiovascular disease
- Significant active or recent infection including tuberculosis
- Previous failure to respond to a TNF alpha antagonist, anakinra or previous treatment with other biological agent
- Severe renal impairment
- Neutropenia

Contacts/Locations

Study Officials: Neil MacKillop, MD PhD
Study Director
AstraZeneca

Locations: India
Research Site
Ahmedabad, Gujarat, India

United States, New York
Research Site
Albany, New York, United States

United States, New Mexico
Research Site
Albuquerque, New Mexico, United States

United States, Alabama
Research Site
Anniston, Alabama, United States

Peru
Research Site
Arequipa, Arequipa, Peru

United States, North Carolina
Research Site
Asheville, North Carolina, United States

United States, Georgia
Research Site
Atlanta, Georgia, United States

Hungary
Research Site
Balatonfured, Hungary

India
Research Site
Bangalore, Karnataka, India

Hungary
Research Site
Bekescsaba, Hungary

United States, Kentucky
Research Site
Bowling Green, Kentucky, United States

Slovakia
Research Site
Bratislava, Slovakia, Slovakia

United States, Connecticut
Research Site

Bridgeport, Connecticut, United States

United States, New York
Research Site
Brooklyn, New York, United States

Belgium
Research Site
Brussels, Belgium

Hungary
Research Site
Budapest, Hungary

Argentina
Research Site
Buenos Aires, Caba, Argentina

Poland
Research Site
Bytom, Poland

Argentina
Research Site
Caba, Argentina

Australia, Queensland
Research Site
Cairns, Queensland, Australia

Australia, New South Wales
Research Site
Camperdown, New South Wales, Australia

United States, South Carolina
Research Site
Charleston, South Carolina, United States

Poland
Research Site
Chelm Slaski, Poland

Mexico
Research Site
Chihuahua, Chihuahua, Mexico

United Kingdom
Research Site
Christchurch, United Kingdom

Argentina
Research Site
Ciudad Autonoma Bs As, CBA, Argentina

United States, Colorado
Research Site
Colorado Springs, Colorado, United States

Argentina
Research Site
Cordoba, CRD, Argentina

Brazil
Research Site
Curitiba, PR, Brazil

United States, Texas
Research Site
Dallas, Texas, United States

United States, Florida
Research Site
Daytona Beach, Florida, United States

Hungary
Research Site
Debrecen, Hungary

Ukraine
Research Site
Donetsk, Ukraine

United States, Pennsylvania
Research Site
Erie, Pennsylvania, United States

United States, Missouri
Research Site
Florissant, Missouri, United States

United States, Mississippi
Research Site

Flowood, Mississippi, United States

United States, North Carolina
Research Site
Greensboro, North Carolina, United States

Poland
Research Site
Grodzisk Mazowiecki, Poland

Mexico
Research Site
Guadalajara, JAL, Mexico

United States, Tennessee
Research Site
Hixson, Tennessee, United States

United States, Texas
Research Site
Houston, Texas, United States

United States, California
Research Site
Huntington Beach, California, United States

United States, Alabama
Research Site
Huntsville, Alabama, United States

India
Research Site
Hyderabad, India

United States, Idaho
Research Site
Idaho Falls, Idaho, United States

United Kingdom
Research Site
Ipswich, United Kingdom

Ukraine
Research Site
Ivano-frankivsk, Ukraine

United States, Montana
Research Site
Kalispell, Montana, United States

Poland
Research Site
Katowice, Poland

Ukraine
Research Site
Kharkiv, Ukraine

Research Site
Kiev, Ukraine

Poland
Research Site
Krakow, Poland

Ukraine
Research Site
Kyiv, Ukraine

United States, Oregon
Research Site
Lake Oswego, Oregon, United States

United States, Delaware
Research Site
Lewes, Delaware, United States

Peru
Research Site
Lima, Lima, Peru

United Kingdom
Research Site
London, United Kingdom

United States, California
Research Site
Long Beach, California, United States

India
Research Site
Lucknow, Uttar Pradesh, India

Ukraine
Research Site
Lviv, Ukraine

Hungary
Research Site
Mako, Hungary

India
Research Site
Mangalore, Karnataka, India

United States, Georgia
Research Site
Marietta, Georgia, United States

United States, Tennessee
Research Site
Memphis, Tennessee, United States

United States, Texas
Research Site
Mesquite, Texas, United States

Mexico
Research Site
Mexicali, Mexico

Research Site
Mexico, Distrito Federal, Mexico

Research Site
Monterrey, Nuevo Leon, Mexico

India
Research Site
Nagpur, Maharshtra, India

Mexico
Research Site
Obrergon, SON, Mexico

United States, Florida
Research Site
Ocala, Florida, United States

Ukraine
Research Site
Odessa, Ukraine

United States, New York
Research Site
Olean, New York, United States

France
Research Site
Orleans Cedex 1, France

Chile
Research Site
Osorno, X Region, Chile

France
Research Site
Paris Cedex 13, France

Estonia
Research Site
Parnu, Estonia

United States, Ohio
Research Site
Perrysburg, Ohio, United States

Bulgaria
Research Site
Plovdiv, Bulgaria

Slovakia
Research Site
Poprad, Slovakia

Peru
Research Site
Pueblo Libre, Lima, Peru

Argentina
Research Site
Quilmes, Argentina

Research Site
Reading, Berkshire, Argentina

Brazil
Research Site
Recife, PE, Brazil

United States, Missouri
Research Site
Richmond Heights, Missouri, United States

Slovakia
Research Site
Rimavska Sobota, Slovakia

Brazil
Research Site
Rio de Janeiro, Brazil

Argentina
Research Site
Rosario, Santa Fe, Argentina

Mexico
Research Site
Saltillo, Coahuila, Mexico

United States, Texas
Research Site
San Antonio, Texas, United States

Argentina
Research Site
San Juan, San Juan, Argentina

Mexico
Research Site
San Luis Potosi, Mexico, Mexico

Argentina
Research Site
San Miguel de Tucuman, TUC, Argentina

United States, California
Research Site
Santa Maria, California, United States

Research Site
Santa Monica, California, United States

Chile
Research Site
Santiago, Chile

Brazil
Research Site
Sao Paulo, SP, Brazil

India
Research Site
Secunderabad, Andhra Pradesh, India

Bulgaria
Research Site
Sevlievo, Bulgaria

Research Site
Sofia, Bulgaria

Hungary
Research Site
Sopron, Hungary

Australia, Queensland
Research Site
Southport, Queensland, Australia

United States, Illinois
Research Site
Springfield, Illinois, United States

United States, Missouri
Research Site
St Louis, Missouri, United States

Hungary
Research Site
Szentes, Hungary

Estonia
Research Site
Tallinn, Estonia

Research Site
Tartu, Estonia

United States, Arizona
Research Site
Tucson, Arizona, United States

United States, Alabama
Research Site
Tuscaloosa, Alabama, United States

India
Research Site
Udupi, Karnataka, India

Bulgaria
Research Site
Veliko Tarnovo, Bulgaria

Ukraine
Research Site
Vinnytsya, Ukraine

India
Research Site
Vishakhapatnam, Andhra Pradesh, India

Brazil
Research Site
Vitoria, ES, Brazil

United Kingdom
Research Site
Warrington, Cheshire, United Kingdom

Poland
Research Site
Warszawa, Poland

United States, Pennsylvania
Research Site
Waxford, Pennsylvania, United States

United Kingdom
Research Site
Westcliff-on-the Sea, United Kingdom

United States, Kansas
Research Site

Wichita, Kansas, United States

United Kingdom
Research Site
Wirral, United Kingdom

Poland
Research Site
Wroclaw, Poland

Belgium
Research Site
Yvoir, Belgium

Hungary
Research Site
Zalaegerszeg-pozva, Hungary

Ukraine
Research Site
Zaporyzhzhya, Ukraine

Slovakia
Research Site
Zilina, Slovakia, Slovakia

Poland
Research Site
Zyrardow, Poland

India
Research Site
Calcutta, India

References

Citations:

Links: URL: http://www.oskirastudy.com
Description Aimed at US participants

Study Data/Documents:

Participant Flow

Recruitment Details	A total of 1475 patients were enrolled: 311, 306 & 306 were randomised to Groups A, B & C, respectively (310, 304 & 304 received at least 1 dose of IP).
Pre-Assignment Details	A total of 552 patients failed screening.

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Overall Study

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Started	310 [1]	304 [1]	304 [1]
Randomised But Did Not Receive Treatment	1 [2]	2 [3]	2 [4]
Completed	207 [5]	191 [5]	161 [5]
Not Completed	103	113	143
Not reported	24	25	21
Enrolment in long term extension	42	36	87
Severe non-compliance to protocol	1	3	3
Lack of therapeutic response	2	3	4
Dev. of study specific discont. criteria	6	16	2
Lost to Follow-up	3	2	2
Adverse Event	25	28	24

[1] Patients who received treatment
[2] Eligibility criteria not fulfilled

[3] Eligibility criteria not fulfilled/other
[4] Adverse event/eligibility criteria not fulfilled
[5] Number of patients who completed treatment includes patients who had a dose reduction.

Baseline Characteristics

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Baseline Measures

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Total
Number of Participants	310	304	304	918
Age, Continuous [units: years] Mean (Standard Deviation)	52 (12.2)	52 (12.0)	53 (11.9)	52 (12.0)
Gender, Male/Female [units: Participants]				
Female	263	254	253	770
Male	47	50	51	148
Race/Ethnicity, Customized [units: Participants]				
White	218	213	209	640
Black or African American	9	5	11	25
Asian	3	10	5	18
American Indian or Alaska Native	14	12	11	37
Indian or Pakistani	20	14	19	53
Other	46	50	49	145

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Proportion of Patients With ACR20 at Week 24, Comparison Between Fostamatinib and Placebo.
Measure Description	ACR20: American College of Rheumatology 20% response criteria, based on count of swollen and tender joints (out of 28 joints), blood test measures of inflammation (such as CRP) and the physician and patient's own assessments of disease activity, pain and physical function. Non-responder imputation has been applied by carrying the baseline observation forward. BID=twice daily, CRP=C-reactive protein, DMARD=disease-modifying anti-rheumatic drug, PO=orally, QD=once a day.
Time Frame	24 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle.

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	310	304	304
Proportion of Patients With ACR20 at Week 24, Comparison Between Fostamatinib and Placebo. [units: Percentage of responders]	49.0	44.4	34.2

Statistical Analysis 1 for Proportion of Patients With ACR20 at Week 24, Comparison Between Fostamatinib and Placebo.

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO

	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Week 24
	Method	Mantel Haenszel
	Comments	Treatment difference in proportion of responders with a Mantel Haenszel approach stratified by pooled country.

Method of Estimation	Estimation Parameter	Other [Weighted difference in proportions]
	Estimated Value	0.15
	Confidence Interval	(2-Sided) 95% 0.08 to 0.22
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Proportion of Patients With ACR20 at Week 24, Comparison Between Fostamatinib and Placebo.

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.006
	Comments	Week 24
	Method	Mantel Haenszel
	Comments	Treatment difference in proportion of responders with a Mantel Haenszel approach stratified by pooled country.

Method of Estimation	Estimation Parameter	Other [Weighted difference in proportions]
	Estimated Value	0.10
	Confidence Interval	(2-Sided) 95% 0.03 to 0.18
	Estimation Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	Change From Baseline to Week 24 in mTSS, Comparison Between Fostamatinib and Placebo.
Measure Description	mTSS: modified total Sharp score, a measure of structural progression based upon X-rays. Hand and foot joints are scored for erosions and joint space narrowing and the results summed to give a value between 0 and 448. A higher value represents more serious progression of the disease. After disregarding ineligible records, patients with 2 or more non-missing values have had missing data imputed via linear extrapolation/interpolation methods. Patients with only 1 result have been excluded from the analysis. ANCOVA=analysis of covariance, BID=twice daily, DMARD=disease-modifying anti-rheumatic drug, IP=investigational product, PO=orally, QD=once a day.
Time Frame	Baseline and 24 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of IP. Patients were analysed by randomised treatment. Measurements at 2 timepoints are required in order for a patient to be included in the analysis; therefore patients with only 1 result have been excluded from the analysis population.

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	285	277	278
Change From Baseline to Week 24 in mTSS, Comparison Between Fostamatinib and Placebo.	0.45 (2.201)	1.29 (13.380)	0.13 (2.142)

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
[units: Units on a scale] Mean (Standard Deviation)			

Statistical Analysis 1 for Change From Baseline to Week 24 in mTSS, Comparison Between Fostamatinib and Placebo.

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	This analysis is performed using an ANCOVA model on the ranks of the change from baseline, by pooled country, including a term for the ranks of the baseline score as a covariate.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.252
	Comments	Week 24
	Method	Cochran-Mantel-Haenszel
	Comments	The residuals from the ANCOVA are analysed using a Cochran-Mantel-Haenszel approach, adjusting for the effects of pooled country.

Statistical Analysis 2 for Change From Baseline to Week 24 in mTSS, Comparison Between Fostamatinib and Placebo.

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	This analysis is performed using an ANCOVA model on the ranks of the change from baseline, by pooled country, including a term for the ranks of the baseline score as a covariate.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.170
	Comments	Week 24
	Method	Cochran-Mantel-Haenszel

	Comments	The residuals from the ANCOVA are analysed using a Cochran-Mantel-Haenszel approach, adjusting for the effects of pooled country.

3. Secondary Outcome Measure:

Measure Title	ACR20 - Proportion of Patients Achieving ACR20, Comparison Between Fostamatinib and Placebo at Week 1
Measure Description	ACR20: American College of Rheumatology 20% response criteria, based on count of swollen and tender joints (out of 28 joints), blood test measures of inflammation (such as CRP) and the physician and patient's own assessments of disease activity, pain and physical function. Non-responder imputation has been applied by carrying the baseline observation forward. BID=twice daily, CRP=C-reactive protein, DMARD=Disease-modifying anti-rheumatic drug, PO=orally.
Time Frame	1 week
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle.

Reporting Groups

	Description
FOSTA 100 MG BID (Combined)	Dosing Group A and B combined
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID (Combined)	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	614	304
ACR20 - Proportion of Patients Achieving ACR20, Comparison Between Fostamatinib and Placebo at Week 1 [units: Percentage of responders]	18.2	4.9

Statistical Analysis 1 for ACR20 - Proportion of Patients Achieving ACR20, Comparison Between Fostamatinib and Placebo at Week 1

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (Combined), PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO

	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Mantel Haenszel
	Comments	95% confidence intervals and p-values are calculated using a Mantel Haenszel approach stratified by pooled country.

Method of Estimation	Estimation Parameter	Other [Weighted difference in proportion]
	Estimated Value	0.13
	Confidence Interval	(2-Sided) 95% 0.10 to 0.17
	Estimation Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Proportion of Patients Achieving ACR50 up to Week 24
Measure Description	ACR50: American College of Rheumatology 50% response criteria, based on count of swollen and tender joints (out of 28 joints), blood test measures of inflammation (such as CRP) and the physician and patient's own assessments of disease activity, pain and physical function. Non-responder imputation has been applied by carrying the baseline observation forward. BID=twice daily, CRP=C-reactive protein, DMARD=Disease-modifying anti-rheumatic drug, PO=orally, QD=once a day.
Time Frame	24 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle.

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	310	304	304
Proportion of Patients Achieving ACR50 up to Week 24 [units: Percentage of responders]	26.1	18.4	9.9

Statistical Analysis 1 for Proportion of Patients Achieving ACR50 up to Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Mantel Haenszel
	Comments	95% confidence intervals and p-values are calculated using a Mantel Haenszel approach stratified by pooled country.

Method of Estimation	Estimation Parameter	Other [Weighted difference in proportions]
	Estimated Value	0.16

	Confidence Interval	(2-Sided) 95% 0.11 to 0.22
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Proportion of Patients Achieving ACR50 up to Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.002
	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Mantel Haenszel
	Comments	95% confidence intervals and p-values are calculated using a Mantel Haenszel approach stratified by pooled country.

Method of Estimation	Estimation Parameter	Other [Weighted difference in proportions]
	Estimated Value	0.09
	Confidence Interval	(2-Sided) 95% 0.03 to 0.14
	Estimation Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Proportion of Patients Achieving ACR70 up to Week 24
Measure Description	ACR70: American College of Rheumatology 70% response criteria, based on count of swollen and tender joints (out of 28 joints), blood test measures of inflammation (such as CRP) and the physician and patient's own assessments of disease activity, pain and physical function. Non-responder imputation has been applied by carrying the baseline observation forward. BID=twice daily, CRP=C-reactive protein, DMARD=Disease-modifying anti-rheumatic drug, PO=orally, QD=once a day.

Time Frame	24 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle.

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	310	304	304
Proportion of Patients Achieving ACR70 up to Week 24 [units: Percentage of responders]	10.3	5.6	2.0

Statistical Analysis 1 for Proportion of Patients Achieving ACR70 up to Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001

	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Mantel Haenszel
	Comments	95% confidence intervals and p-values are calculated using a Mantel Haenszel approach stratified by pooled country.

Method of Estimation	Estimation Parameter	Other [Weighted difference in proportions]
	Estimated Value	0.08
	Confidence Interval	(2-Sided) 95% 0.05 to 0.12
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Proportion of Patients Achieving ACR70 up to Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.015
	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Mantel Haenszel
	Comments	95% confidence intervals and p-values are calculated using a Mantel Haenszel approach stratified by pooled country.

Method of Estimation	Estimation Parameter	Other [Weighted difference in proportions]
	Estimated Value	0.04
	Confidence Interval	(2-Sided) 95% 0.01 to 0.07
	Estimation Comments	[Not specified]

6. Secondary Outcome Measure:

Measure Title	ACRn - Comparison Between Fostamatinib and Placebo at Week 24
Measure Description	ACRn: American College of Rheumatology index of RA improvement, based on smallest percentage improvement in the count of swollen joints (out of 28 joints), count of tender joints (out of 28 joints), or in blood test measures of inflammation (such as CRP) or the physician or patient's own assessments of disease activity, pain and physical function. Scores are reported as a percentage improvement on a scale of -100 to +100, with larger values representing a better clinical outcome. BID=twice daily, CI=confidence interval, CRP=C-reactive protein, DMARD=Disease-modifying anti-rheumatic drug, PO=orally, QD=once a day, RA=rheumatoid arthritis. Mean refers to change at Week 24.
Time Frame	24 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle.

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	310	304	304
ACRn - Comparison Between Fostamatinib and Placebo at Week 24 [units: Percentage improvement from baseline] Mean (Standard Deviation)	26.13 (30.833)	20.06 (28.599)	12.92 (26.611)

Statistical Analysis 1 for ACRn - Comparison Between Fostamatinib and Placebo at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Nominal p-value presented for treatment comparison. ACRn was not formally tested within the predefined multiplicity procedure. As this is a non-parametric test p-values alone are presented rather than an estimated treatment difference.
	Method	Other [Van Elteren]
	Comments	The treatment differences, 95% CIs and p-values are estimated using the Van Elteren test stratified by pooled country.

Statistical Analysis 2 for ACRn - Comparison Between Fostamatinib and Placebo at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.002
	Comments	Nominal p-value presented for treatment comparison. ACRn was not formally tested within the predefined multiplicity procedure. As this is a non-parametric test p-values alone are presented rather than an estimated treatment difference.
	Method	Other [Van Elteren]
	Comments	The treatment differences, 95% CIs and p-values are estimated using the Van Elteren test stratified by pooled country.

7. Secondary Outcome Measure:

Measure Title	Proportion of Patients Achieving DAS28-CRP <2.6 at Week 12
Measure Description	DAS28-CRP: Disease Activity Score based on a count of swollen and tender joints (out of 28 joints), blood test measures of inflammation (CRP) and the patient's own assessment. Scores can take any positive value with a lower value indicating a better clinical condition. A DAS28-CRP score of <2.6 is indicative of remission of RA symptoms. BID=twice daily, CRP=C-reactive protein, DMARD=Disease-modifying anti-rheumatic drug, OR=odds ratio, PO=orally, QD=once a day.
Time Frame	12 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle.

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	310	304	304
Proportion of Patients Achieving DAS28-CRP <2.6 at Week 12 [units: Percentage of responders]	10.3	7.9	2.0

Statistical Analysis 1 for Proportion of Patients Achieving DAS28-CRP <2.6 at Week 12

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Regression, Logistic
	Comments	Odds ratio and 95% confidence intervals are calculated using Logistic Regression with treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	6.0
	Confidence Interval	(2-Sided) 95% 2.44 to 14.64
	Estimation Comments	An odds ratio >1 indicates a benefit towards Fostamatinib.

Statistical Analysis 2 for Proportion of Patients Achieving DAS28-CRP <2.6 at Week 12

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.002
	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Regression, Logistic
	Comments	Odds ratio and 95% confidence intervals are calculated using Logistic Regression with treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	4.4
	Confidence Interval	(2-Sided) 95% 1.76 to 11.02
	Estimation Comments	An odds ratio >1 indicates a benefit towards Fostamatinib.

8. Secondary Outcome Measure:

Measure Title	Proportion of Patients Achieving DAS28-CRP <2.6 at Week 24
Measure Description	DAS28-CRP: Disease Activity Score based on a count of swollen and tender joints (out of 28 joints), blood test measures of inflammation (CRP) and the patient's own assessment. Scores can take any positive value with a lower value indicating a better clinical condition. A DAS28-CRP score of <2.6 is indicative of remission of RA symptoms. BID=twice daily, CRP=C-reactive protein, DMARD=Disease-modifying anti-rheumatic drug, OR=odds ratio, PO=orally, QD=once a day.
Time Frame	24 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle.

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	310	304	304
Proportion of Patients Achieving DAS28-CRP <2.6 at Week 24 [units: Percentage of responders]	13.2	8.6	4.9

Statistical Analysis 1 for Proportion of Patients Achieving DAS28-CRP <2.6 at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Regression, Logistic
	Comments	Odds ratio and 95% confidence intervals are calculated using Logistic Regression with treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	3.0
	Confidence Interval	(2-Sided) 95% 1.63 to 5.67
	Estimation Comments	An odds ratio >1 indicates a benefit towards Fostamatinib.

Statistical Analysis 2 for Proportion of Patients Achieving DAS28-CRP <2.6 at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.083
	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Regression, Logistic
	Comments	Odds ratio and 95% confidence intervals are calculated using Logistic Regression with treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.8
	Confidence Interval	(2-Sided) 95% 0.93 to 3.50
	Estimation Comments	An odds ratio >1 indicates a benefit towards Fostamatinib.

9. Secondary Outcome Measure:

Measure Title	Proportion of Patients Achieving DAS28-CRP EULAR Response at Week 24
Measure Description	Change in DAS28 was derived for each post baseline scheduled assessment and categorised using the European League Against Rheumatism (EULAR) response criteria. Non-responder imputation has been applied by carrying the baseline observation forward. BID=twice daily, CRP=C-reactive protein, DAS28=Disease Activity Score based on a 28-joint count, DMARD=disease-modifying anti-rheumatic drug, OR=odds ratio, PO=orally, QD=once a day.
Time Frame	24 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle.

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	310	304	304
Proportion of Patients Achieving DAS28-CRP EULAR Response at Week 24 [units: Percentage of responders]			
No response	34.8	41.1	53.0
Moderate response	39.0	44.4	36.2
Good response	26.1	14.5	10.9

Statistical Analysis 1 for Proportion of Patients Achieving DAS28-CRP EULAR Response at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Nominal p-value presented for treatment comparison. This was not formally tested within the predefined multiplicity procedure.
	Method	Other [Proportional odds model]
	Comments	No response, moderate response and good response are included in the proportional odds model with treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	2.43
	Confidence Interval	(2-Sided) 95% 1.79 to 3.30
	Estimation Comments	An odds ratio >1 indicates a benefit towards fostamatinib.

Statistical Analysis 2 for Proportion of Patients Achieving DAS28-CRP EULAR Response at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.004
	Comments	Nominal p-value presented for treatment comparison. This was not formally tested within the predefined multiplicity procedure.
	Method	Other [Proportional odds model]
	Comments	No response, moderate response and good response are included in the proportional odds model with treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.57
	Confidence Interval	(2-Sided) 95% 1.16 to 2.14
	Estimation Comments	An odds ratio >1 indicates a benefit towards Fostamatinib.

10. Secondary Outcome Measure:

Measure Title	HAQ-DI Response - Comparison of the Change (>=0.22) From Baseline Between Fostamatinib and Placebo at Week 24
Measure Description	HAQ-DI: Health Assessment Questionnaire – Disability Index, a measure of physical function. The HAQ-DI score is calculated by summing scores from 8 sub-categories (ie, scores for patient ability in dressing and grooming, rising, eating, walking, hygiene, reach, grip and common daily activities) and dividing by the number of categories completed. The HAQ-DI score takes values between 0 and 3, with higher score indicating greater disability. HAQ-DI response: a reduction from baseline in HAQ-DI greater than or equal to the minimally important difference (0.22). BID=twice daily, DMARD=disease-modifying anti-rheumatic drug, OR=odds ratio, PO=orally, QD=once a day.
Time Frame	Baseline and 24 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle.

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	310	304	304
HAQ-DI Response - Comparison of the Change (>=0.22) From Baseline Between Fostamatinib and Placebo at Week 24 [units: Percentage of responders]	54.8	50.3	35.2

Statistical Analysis 1 for HAQ-DI Response - Comparison of the Change (>=0.22) From Baseline Between Fostamatinib and Placebo at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Regression, Logistic

	Comments	Odds ratio and 95% confidence intervals are calculated using Logistic Regression with treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	2.3
	Confidence Interval	(2-Sided) 95% 1.68 to 3.26
	Estimation Comments	An odds ratio >1 indicates a benefit towards Fostamatinib.

Statistical Analysis 2 for HAQ-DI Response - Comparison of the Change (>=0.22) From Baseline Between Fostamatinib and Placebo at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Nominal p-values presented. Formal statistical testing could not be carried out due to the predefined multiplicity procedure (as the primary variable comparisons were non-significant).
	Method	Regression, Logistic
	Comments	Odds ratio and 95% confidence intervals are calculated using Logistic Regression with treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.9
	Confidence Interval	(2-Sided) 95% 1.38 to 2.68
	Estimation Comments	An odds ratio >1 indicates a benefit towards Fostamatinib.

11. Secondary Outcome Measure:

Measure Title	SF-36 - Comparison of the Change in PCS From Baseline Between Fostamatinib and Placebo at Week 24

Measure Description	SF-36: 36 item Short Form Health Survey, a measure of health-related QoL. Scores for 8 sub-domains (Physical Functioning, Role-physical, Bodily Pain, General Health, Vitality, Social Function, Role-emotional & Mental Health) are derived & normalised to a scale of 0-100. Physical Component Scores (PCS) are derived by multiplying each of these 8 scores by a constant, summing them & standardising against a population with mean of 50, standard deviation of 10. Higher scores represent a better QoL. Mean changes from baseline score are presented at each visit as increases from baseline (defined as post-baseline minus baseline); larger changes indicate a better clinical condition. ANCOVA=analysis of covariance, BID=twice daily, DMARD=disease modifying antirheumatic drug, PO=orally, QD=once daily, QoL=quality of life.
Time Frame	Baseline and 24 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	310	304	303
SF-36 - Comparison of the Change in PCS From Baseline Between Fostamatinib and Placebo at Week 24 [units: Units on a scale] Mean (Standard Deviation)	6 (8.0)	5 (6.7)	3 (6.2)

Statistical Analysis 1 for SF-36 - Comparison of the Change in PCS From Baseline Between Fostamatinib and Placebo at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO

	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	Nominal p-value presented for treatment comparison. This was not formally tested within the predefined multiplicity procedure.
	Method	ANCOVA
	Comments	Including terms for baseline as a continuous covariate and treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Other [Treatment difference]
	Estimated Value	2.24
	Confidence Interval	(2-Sided) 95% 1.16 to 3.31
	Estimation Comments	[Not specified]

Statistical Analysis 2 for SF-36 - Comparison of the Change in PCS From Baseline Between Fostamatinib and Placebo at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.020
	Comments	Nominal p-value presented for treatment comparison. This was not formally tested within the predefined multiplicity procedure.
	Method	ANCOVA
	Comments	Including terms for baseline as a continuous covariate and treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Other [Treatment difference]
	Estimated Value	1.27
	Confidence Interval	(2-Sided) 95% 0.20 to 2.35
	Estimation Comments	[Not specified]

12. Secondary Outcome Measure:

Measure Title	SF-36 - Comparison of the Change in MCS From Baseline Between Fostamatinib and Placebo at Week 24
Measure Description	SF-36: 36 item Short Form Health Survey, a measure of health-related QoL. Scores for 8 sub-domains (Physical Functioning, Role-physical, Bodily Pain, General Health, Vitality, Social Function, Role-emotional & Mental Health) are derived & normalised to a scale of 0-100. Mental Component Scores (MCS) are derived by multiplying each of these 8 scores by a constant, summing them & standardising against a population with mean of 50, standard deviation of 10. Higher scores represent a better QoL. Mean changes from baseline score are presented at each visit as increases from baseline (defined as post-baseline minus baseline); larger changes indicate a better clinical condition. ANCOVA=analysis of covariance, BID=twice daily, DMARD=disease modifying antirheumatic drug, PO=orally, QD=once daily, QoL=quality of life.
Time Frame	Baseline and 24 weeks
Safety Issue?	No

Analysis Population Description

The full analysis set includes those patients who received at least 1 dose of investigational product. Patients were analysed by randomised treatment in accordance with the intention to treat principle

Reporting Groups

	Description
FOSTA 100 MG BID PO	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO	Dosing Group C

Measured Values

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
Number of Participants Analyzed	310	304	303

	FOSTA 100 MG BID PO	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO	PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
SF-36 - Comparison of the Change in MCS From Baseline Between Fostamatinib and Placebo at Week 24 [units: Units on a scale] Mean (Standard Deviation)	4 (9.5)	4 (8.6)	2 (8.1)

Statistical Analysis 1 for SF-36 - Comparison of the Change in MCS From Baseline Between Fostamatinib and Placebo at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO
	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.005
	Comments	Nominal p-value presented for treatment comparison. This was not formally tested within the predefined multiplicity procedure.
	Method	ANCOVA
	Comments	Including terms for baseline as a continuous covariate and treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Other [Treatment difference]
	Estimated Value	1.80
	Confidence Interval	(2-Sided) 95% 0.54 to 3.07
	Estimation Comments	[Not specified]

Statistical Analysis 2 for SF-36 - Comparison of the Change in MCS From Baseline Between Fostamatinib and Placebo at Week 24

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID (4 WKS) THEN 150 MG QD PO, PLACEBO (24 WKS) THEN FOSTA 100 MG BID PO

	Comments	Non-responder imputation has been applied following premature withdrawal, or increased dose of methotrexate or any DMARD initiation, or for 8 weeks following receipt of any parenteral steroids, or for patients with no post baseline data.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.017
	Comments	Nominal p-value presented for treatment comparison. This was not formally tested within the predefined multiplicity procedure.
	Method	ANCOVA
	Comments	Including terms for baseline as a continuous covariate and treatment and pooled country as factors.

Method of Estimation	Estimation Parameter	Other [Treatment difference]
	Estimated Value	1.56
	Confidence Interval	(2-Sided) 95% 0.28 to 2.83
	Estimation Comments	[Not specified]

Reported Adverse Events

Time Frame	52 weeks
Additional Description	For placebo treated patients time frame includes both placebo (24 weeks) and fostamatinib (28 weeks) treatment. 5 SAEs occurred during the 24 week placebo treated period.

Reporting Groups

	Description
FOSTA 100 MG BID	Dosing Group A
FOSTA 100 MG BID (4 WKS) THEN 150 MG QD	Dosing Group B
PLACEBO (24 WKS) THEN FOSTA 100 MG BID - FOSTA Period	Dosing Group C

	Description
PLACEBO (24 WKS) THEN FOSTA 100 MG BID - Placebo Period	

Serious Adverse Events

	FOSTA 100 MG BID		FOSTA 100 MG BID (4 WKS) THEN 150 MG QD		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - FOSTA Period		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - Placebo Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	24/310 (7.74%)		24/304 (7.89%)		12/304 (3.95%)		5/304 (1.64%)	
Blood and lymphatic system disorders								
ANAEMIA [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
Cardiac disorders								
ACUTE MYOCARDIAL INFARCTION [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
ATRIAL FIBRILLATION [A] †	0/310 (0%)	0	2/304 (0.66%)	2	1/304 (0.33%)	1	0/304 (0%)	0
ATRIAL FLUTTER [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
ATRIAL THROMBOSIS [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
CARDIAC FAILURE [A] †	0/310 (0%)	0	0/304 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1
CARDIAC FAILURE ACUTE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
CARDIOPULMONARY FAILURE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
Eye disorders								
CHORIORETINOPATHY [A] †	0/310 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0

	FOSTA 100 MG BID		FOSTA 100 MG BID (4 WKS) THEN 150 MG QD		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - FOSTA Period		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - Placebo Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Gastrointestinal disorders								
COLITIS [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
COLONIC OBSTRUCTION [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
DUODENAL ULCER HAEMORRHAGE [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
GASTRITIS ATROPHIC [A] †	0/310 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0
PANCREATITIS [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
REFLUX GASTRITIS [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
Hepatobiliary disorders								
BILE DUCT OBSTRUCTION [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
BILIARY COLIC [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
CHOLECYSTITIS [A] †	1/310 (0.32%)	1	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
CHOLELITHIASIS [A] †	2/310 (0.65%)	2	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
Immune system disorders								
ANAPHYLACTIC REACTION [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
Infections and infestations								
APPENDICITIS [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0

	FOSTA 100 MG BID		FOSTA 100 MG BID (4 WKS) THEN 150 MG QD		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - FOSTA Period		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - Placebo Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
BACTERIAL DIARRHOEA [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
BRONCHITIS [A] †	0/310 (0%)	0	1/304 (0.33%)	1	1/304 (0.33%)	1	0/304 (0%)	0
CELLULITIS [A] †	2/310 (0.65%)	2	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
ESCHERICHIA URINARY TRACT INFECTION [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
GASTROENTERITIS [A] †	1/310 (0.32%)	1	3/304 (0.99%)	3	0/304 (0%)	0	0/304 (0%)	0
GASTROENTERITIS VIRAL [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
PANCREATITIS VIRAL [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
PNEUMONIA [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
PULMONARY TUBERCULOSIS [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
SEPSIS [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
SEPTIC SHOCK [A] †	0/310 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0
UPPER RESPIRATORY TRACT INFECTION [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
URINARY TRACT INFECTION [A] †	0/310 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0
Injury, poisoning and procedural complications								

	FOSTA 100 MG BID		FOSTA 100 MG BID (4 WKS) THEN 150 MG QD		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - FOSTA Period		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - Placebo Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
ACCIDENTAL OVERDOSE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
CONTUSION [A] †	0/310 (0%)	0	0/304 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1
FEMORAL NECK FRACTURE [A] †	0/310 (0%)	0	0/304 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1
FEMUR FRACTURE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
FIBULA FRACTURE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
HIP FRACTURE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
HUMERUS FRACTURE [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
SPINAL FRACTURE [A] †	0/310 (0%)	0	0/304 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1
TIBIA FRACTURE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
Metabolism and nutrition disorders								
DEHYDRATION [A] †	0/310 (0%)	0	0/304 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1
Musculoskeletal and connective tissue disorders								
FOOT DEFORMITY [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
OSTEOARTHRITIS [A] †	1/310 (0.32%)	1	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0
PATHOLOGICAL FRACTURE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0

	FOSTA 100 MG BID		FOSTA 100 MG BID (4 WKS) THEN 150 MG QD		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - FOSTA Period		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - Placebo Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
RHEUMATOID ARTHRITIS [A] †	2/310 (0.65%)	2	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0
SPONDYLOLISTHESIS [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
SYSTEMIC LUPUS ERYTHEMATOSUS [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)								
BASAL CELL CARCINOMA [A] †	0/310 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0
GANGLIONEUROMA [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
GASTRIC CANCER [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
RENAL CANCER [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
THYROID CANCER [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
UTERINE LEIOMYOMA [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
Nervous system disorders								
ISCHAEMIC STROKE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
MULTIPLE SCLEROSIS [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
TRANSIENT GLOBAL AMNESIA [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
Pregnancy, puerperium and perinatal conditions								

	FOSTA 100 MG BID		FOSTA 100 MG BID (4 WKS) THEN 150 MG QD		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - FOSTA Period		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - Placebo Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
ABORTION SPONTANEOUS [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
Psychiatric disorders								
CONFUSIONAL STATE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
Renal and urinary disorders								
CALCULUS URINARY [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
NEPHROLITHIASIS [A] †	0/310 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0
RENAL ARTERY STENOSIS [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
RENAL FAILURE ACUTE [A] †	0/310 (0%)	0	1/304 (0.33%)	1	1/304 (0.33%)	1	0/304 (0%)	0
Reproductive system and breast disorders								
HAEMORRHAGIC OVARIAN CYST [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
METRORRHAGIA [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
Respiratory, thoracic and mediastinal disorders								
ACUTE RESPIRATORY FAILURE [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
DYSPNOEA [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
INTERSTITIAL LUNG DISEASE [A] †	0/310 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0

	FOSTA 100 MG BID		FOSTA 100 MG BID (4 WKS) THEN 150 MG QD		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - FOSTA Period		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - Placebo Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
PULMONARY EMBOLISM [A] †	0/310 (0%)	0	0/304 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1
Skin and subcutaneous tissue disorders								
ANGIOEDEMA [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
VITILIGO [A] †	1/310 (0.32%)	1	0/304 (0%)	0	0/304 (0%)	0	0/304 (0%)	0
Vascular disorders								
CIRCULATORY COLLAPSE [A] †	0/310 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0
HYPOTENSION [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
HYPOVOLAEMIC SHOCK [A] †	0/310 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0	0/304 (0%)	0
PERIPHERAL ISCHAEMIA [A] †	0/310 (0%)	0	0/304 (0%)	0	1/304 (0.33%)	1	0/304 (0%)	0

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 15.1

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	FOSTA 100 MG BID		FOSTA 100 MG BID (4 WKS) THEN 150 MG QD		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - FOSTA Period		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - Placebo Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	169/310 (54.52%)		191/304 (62.83%)		64/304 (21.05%)		80/304 (26.32%)	
Gastrointestinal disorders								
ABDOMINAL PAIN UPPER [A] †	12/310 (3.87%)	12	16/304 (5.26%)	17	3/304 (0.99%)	3	10/304 (3.29%)	10
DIARRHOEA [A] †	60/310 (19.35%)	84	63/304 (20.72%)	87	18/304 (5.92%)	26	12/304 (3.95%)	14
NAUSEA [A] †	19/310 (6.13%)	20	27/304 (8.88%)	31	8/304 (2.63%)	9	11/304 (3.62%)	11
VOMITING [A] †	18/310 (5.81%)	18	8/304 (2.63%)	9	5/304 (1.64%)	6	5/304 (1.64%)	5
Infections and infestations								
NASOPHARYNGITIS [A] †	22/310 (7.1%)	29	28/304 (9.21%)	34	6/304 (1.97%)	7	11/304 (3.62%)	14
URINARY TRACT INFECTION BACTERIAL [A] †	18/310 (5.81%)	23	14/304 (4.61%)	19	6/304 (1.97%)	6	6/304 (1.97%)	6
Investigations								
ALANINE AMINOTRANSFERASE INCREASED [A] †	22/310 (7.1%)	27	22/304 (7.24%)	23	8/304 (2.63%)	10	5/304 (1.64%)	6
ASPARTATE AMINOTRANSFERASE INCREASED [A] †	16/310 (5.16%)	18	13/304 (4.28%)	15	4/304 (1.32%)	7	5/304 (1.64%)	7
BLOOD PRESSURE INCREASED [A] †	17/310 (5.48%)	18	16/304 (5.26%)	23	4/304 (1.32%)	4	5/304 (1.64%)	5
Musculoskeletal and connective tissue disorders								
BACK PAIN [A] †	18/310 (5.81%)	19	8/304 (2.63%)	8	2/304 (0.66%)	3	2/304 (0.66%)	2

	FOSTA 100 MG BID		FOSTA 100 MG BID (4 WKS) THEN 150 MG QD		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - FOSTA Period		PLACEBO (24 WKS) THEN FOSTA 100 MG BID - Placebo Period	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
RHEUMATOID ARTHRITIS [A] †	16/310 (5.16%)	18	8/304 (2.63%)	9	6/304 (1.97%)	6	12/304 (3.95%)	13
Nervous system disorders								
HEADACHE [A] †	15/310 (4.84%)	20	20/304 (6.58%)	29	7/304 (2.3%)	7	12/304 (3.95%)	12
Vascular disorders								
HYPERTENSION [A] †	59/310 (19.03%)	72	58/304 (19.08%)	76	11/304 (3.62%)	13	12/304 (3.95%)	12

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 15.1

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There is NOT an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

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