ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 04/23/2014

ClinicalTrials.gov ID: NCT01563978

Study Identification

Unique Protocol ID:	D4300C00033
Brief Title:	Study of the Effect of Fostamatinib Twice Daily on Blood Pressure in Patients With Rheumatoid Arthritis (Oskira ABPM)
Official Title:	OSKIRA-ABPM: A Multi-Centre, Randomised, Double-Blind, Placebo-Controlled, Parallel Group Study of the Effect of Fostamatinib 100 mg Twice Daily on 24-hour Ambulatory Blood Pressure in Patients With Rheumatoid Arthritis
Secondary IDs:	2011-006070-73

Study Status

Record Verification:	April 2014
Overall Status:	Completed
Study Start:	April 2012
Primary Completion:	January 2013 [Actual]
Study Completion:	January 2013 [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: Not yet assigned 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 Bulgaria: Bulgarian Drug Agency Ministry of Health (BDA) Czech Republic: The State Institute for Drug Control Poland: Office for Registration of Medicinal Products, Medical Devices and Biocides Ukraine: Ministry of Public Health of Ukraine (MPHU) Germany: Federal Institute for Drugs and Medical Devices (BfArM) South Africa: Medicines Control Council Argentina: National Administration of Drugs, Food & Medical Technology (ANMAT) Mexico: Federal Commission for Protection Against Sanitary Risks (COFEPRIS) Peru: General Directorate of Medicines, Supplies and Drug (DIGEMID) Brazil: The National Health Surveillance Agency (ANVISA)

Study Description

Brief Summary:	The purpose of this study is to evaluate the effect of fostamatinib compared to placebo on ambulatory blood pressure in patients with active rheumatoid arthritis who are taking a disease-modifying anti-rheumatic drug (DMARD). The study will last for 57 days.
Detailed Description:	OSKIRA-ABPM: A Multi-Centre, Randomised, Double-Blind, Placebo-Controlled, Parallel Group Study of the Effect of Fostamatinib 100 mg Twice Daily on 24-hour Ambulatory Blood Pressure in Patients with Rheumatoid Arthritis

Conditions

Conditions:	Rheumatoid Arthritis
Keywords:	Rheumatoid Arthritis

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Parallel Assignment
Number of Arms:	2
Masking:	Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Allocation:	Randomized
Endpoint Classification:	Safety Study
Enrollment:	266 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Dosing Regimen A Oral treatment	Drug: fostamatinib fostamatinib 100 mg twice daily
Placebo Comparator: Dosing Regimen B Oral treatment	Drug: placebo placebo

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	150 Years
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- Male and female patients aged 18 or over diagnosed with rheumatoid arthritis after the age of 16
- Active rheumatoid arthritis defined as: ≥4 swollen joints and ≥4 tender/painful joints (from 28 joint count) and either erythrocyte sedimentation rate ≥28 mm/h, or C-reactive protein ≥10 mg/L.

- Currently taking one of the following disease-modifying anti-rheumatic drugs: methotrexate, sulfasalazine, hydroxychloroquine or chloroquine.
- Patients without essential hypertension or with essential hypertension if their blood pressure is controlled (<140/90 mmHg) with anti-hypertensive medications being stable at least 4 weeks prior to randomisation.

Exclusion Criteria:

- Females who are pregnant or breastfeeding.
- Certain inflammatory conditions (other than rheumatoid arthritis), connective tissue diseases or chronic pain disorders
- History of liver problems that have required previous investigations
- Evidence of tuberculosis infection
- Conditions that preclude or render difficult the 24-hour ambulatory blood pressure monitoring technique.

Contacts/Locations

Study Officials: Chris O'Brien, MD PhD
Study Director
AstraZeneca

Locations: Argentina
Research Site
Buenos Aires, Argentina

Research Site
Caba, Argentina

Research Site
San Miguel de Tucuman, Argentina

Research Site
San Juan, Argentina

Research Site
San Miguel de Tucuman, Argentina

Research Site
Autonoma, Argentina

Research Site
Buenos Aires, Argentina

Research Site
Ciudad Autonoma Bs As, Argentina

Research Site

Ciudad de Buenos Aires, Argentina

Research Site
Buenos Aires, Argentina

Research Site
Quilmes, Argentina

Research Site
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Bulgaria
Research Site
Plovdiv, Bulgaria

Research Site
Sevlievo, Bulgaria

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Sofia, Bulgaria

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Sofia, Bulgaria

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Sofia, Bulgaria

Czech Republic
Research Site
Ostrava-Trebovice, Czech Republic

Research Site
Hlucin, Czech Republic

Research Site
Praha 11, Czech Republic

Research Site
Praha 4, Czech Republic

Research Site
Praha 2, Czech Republic

Research Site
Zlin, Czech Republic

Research Site
Hostivice, Czech Republic

Research Site
Brno, Czech Republic

Research Site
Kladno, Czech Republic

Germany
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Aachen, Germany

Research Site
Köln, Germany

Research Site
Frankfurt, Germany

Research Site
Muenchen, Germany

Research Site
Herne, Germany

Research Site
Halle, Germany

Mexico
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San Luis Potosí, Mexico

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DF, Mexico

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Monterrey, Mexico

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Obrergon, Mexico

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Saltillo, Mexico

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Arequipa, Peru

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Poland
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Wroclaw, Poland

Research Site
Grodzisk Mazowiecki, Poland

Research Site
Wrocław, Poland

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Łódź, Poland

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Sroda Wielkopolska, Poland

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Brzozow, Poland

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Kalisz, Poland

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Katowice, Poland

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Gdynia, Poland

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Poznan, Poland

Ukraine
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Kharkiv, Ukraine

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Research Site
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Worcester, Massachusetts, United States

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Long Beach, California, United States

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

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

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

United States, Tennessee
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Memphis, Tennessee, United States

United States, California
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Santa Maria, California, United States

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Albuquerque, New Mexico, United States

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Research Site
Greensboro, North Carolina, United States

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

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

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

Research Site
San Antonio, Texas, United States

United States, Maryland
Research Site
Frederick, Maryland, United States

United States, Texas
Research Site
Lubbock, Texas, United States

United States, New Jersey
Research Site
Freehold, New Jersey, United States

United States, Washington
Research Site
Tacoma, Washington, United States

United States, South Carolina
Research Site
Orangeburg, South Carolina, United States

United States, Florida
Research Site
Boca Raton, Florida, United States

United States, Connecticut
Research Site
Trumbull, Connecticut, United States

United States, Maryland
Research Site
Hagerstown, Maryland, United States

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

United States, Florida
Research Site
Venice, Florida, United States

United States, Pennsylvania
Research Site
Duncansville, Pennsylvania, United States

United States, Maryland
Research Site
Cumberland, Maryland, United States

United States, Georgia
Research Site
Decatur, Georgia, United States

United States, Florida
Research Site
Tampa, Florida, United States

United States, North Carolina
Research Site
Charlotte, North Carolina, United States

United States, Texas
Research Site

Dallas, Texas, United States

United States, Florida
Research Site
Orlando, Florida, United States

United States, New Mexico
Research Site
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United States, Indiana
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South Bend, Indiana, United States

United States, Texas
Research Site
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United States, Maryland
Research Site
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United States, Texas
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Austin, Texas, United States

Research Site
Nassau Bay, Texas, United States

South Africa
Research Site
Pretoria, South Africa

Research Site
Kempron Park, South Africa

Research Site
Durban, South Africa

Research Site
Cape Town, South Africa

Research Site
Pretoria, South Africa

Research Site
Bloemfontein, South Africa

Research Site
Cape Town, South Africa

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Recruitment Details	A total of 266 patients were enrolled.
Pre-Assignment Details	A total of 131 patients failed screening.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment
PLACEBO	Oral treatment

Overall Study

	FOSTA 100 MG BID	PLACEBO
Started	68 [1]	67 [1]
Randomised But Did Not Receive Treatment	0	0

	FOSTA 100 MG BID	PLACEBO
Completed	64	65
Not Completed	4	2
Physician Decision	1	0
Lost to Follow-up	1	0
Dev. of study specific discont. criteria	1	0
Adverse Event	1	2

[1] Patients who received treatment.

Baseline Characteristics

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment
PLACEBO	Oral treatment

Baseline Measures

	FOSTA 100 MG BID	PLACEBO	Total
Number of Participants	68	67	135
Age, Continuous [units: Years] Mean (Standard Deviation)	54 (12.0)	54 (13.0)	54 (12.5)
Gender, Male/Female [units: Participants]			
Female	57	57	114
Male	11	10	21
Race/Ethnicity, Customized [units: Participants]			
White	63	58	121
Black or African American	3	8	11
Indian or Pakistani	2	1	3

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change From Baseline in 24-hour Mean Ambulatory SBP
Measure Description	ANCOVA=analysis of covariance, BID=twice daily, FAS=full analysis set, IP=investigational product, SBP=systolic blood pressure.
Time Frame	4 weeks
Safety Issue?	Yes

Analysis Population Description

The FAS includes those randomised patients who received at least 1 dose of IP. Patients were analysed by randomised treatment in accordance with the intention to treat principle.The analysis population for each endpoint includes patients from the FAS still on IP at 4 weeks and with a valid measurement for this type of blood pressure assessment.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment
PLACEBO	Oral treatment

Measured Values

	FOSTA 100 MG BID	PLACEBO
Number of Participants Analyzed	64	62
Change From Baseline in 24-hour Mean Ambulatory SBP [units: mmHg] Mean (Standard Deviation)	4.3 (7.34)	1.3 (7.87)

Statistical Analysis 1 for Change From Baseline in 24-hour Mean Ambulatory SBP

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.023
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least squares mean treatment difference]
	Estimated Value	2.93
	Confidence Interval	(2-Sided) 95% 0.40 to 5.45
	Estimation Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Change From Baseline in 24-hour Mean Ambulatory DBP
Measure Description	ANCOVA=analysis of covariance, BID=twice daily, DBP=diastolic blood pressure, FAS=full analysis set, IP=investigational product.
Time Frame	4 weeks
Safety Issue?	Yes

Analysis Population Description

The FAS includes those randomised patients who received at least 1 dose of IP. Patients were analysed by randomised treatment in accordance with the intention to treat principle.The analysis population for each endpoint includes patients from the FAS still on IP at 4 weeks and had a valid measurement for this type of blood pressure assessment.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment
PLACEBO	Oral treatment

Measured Values

	FOSTA 100 MG BID	PLACEBO
Number of Participants Analyzed	64	62
Change From Baseline in 24-hour Mean Ambulatory DBP [units: mmHg]	4.4 (4.67)	0.7 (4.41)

	FOSTA 100 MG BID	PLACEBO
Mean (Standard Deviation)		

Statistical Analysis 1 for Change From Baseline in 24-hour Mean Ambulatory DBP

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least squares mean treatment difference]
	Estimated Value	3.53
	Confidence Interval	(2-Sided) 95% 2.04 to 5.03
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Change From Baseline in Mean Daytime and Night-time SBP and DBP by Ambulatory Blood Pressure Monitoring
Measure Description	ANCOVA=analysis of covariance, BID=twice daily, DBP=diastolic blood pressure, FAS=full analysis set, IP=investigational product, SBP=systolic blood pressure.
Time Frame	4 weeks
Safety Issue?	Yes

Analysis Population Description

The FAS includes those randomised patients who received at least 1 dose of IP. Patients were analysed by randomised treatment in accordance with the intention to treat principle.The analysis population for each endpoint includes patients from the FAS still on IP at 4 weeks and with a valid measurement for this type of blood pressure assessment.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment
PLACEBO	Oral treatment

Measured Values

	FOSTA 100 MG BID	PLACEBO
Number of Participants Analyzed	64	62
Change From Baseline in Mean Daytime and Night-time SBP and DBP by Ambulatory Blood Pressure Monitoring [units: mmHg] Mean (Standard Deviation)		
Day 28 daytime SBP	4.9 (8.44)	1.6 (8.45)
Day 28 daytime DBP	4.7 (5.20)	0.8 (4.89)
Day 28 night-time SBP	3.0 (8.59)	0.9 (9.75)
Day 28 night-time DBP	3.7 (6.04)	0.8 (6.46)

Statistical Analysis 1 for Change From Baseline in Mean Daytime and Night-time SBP and DBP by Ambulatory Blood Pressure Monitoring

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in mean daytime SBP (Day 28)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.020
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	3.30

	Confidence Interval	(2-Sided) 95% 0.53 to 6.08
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Change From Baseline in Mean Daytime and Night-time SBP and DBP by Ambulatory Blood Pressure Monitoring

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in mean daytime DBP (Day 28)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	3.75
	Confidence Interval	(2-Sided) 95% 2.08 to 5.42
	Estimation Comments	[Not specified]

Statistical Analysis 3 for Change From Baseline in Mean Daytime and Night-time SBP and DBP by Ambulatory Blood Pressure Monitoring

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in mean night-time SBP (Day 28)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.179
	Comments	[Not specified]
	Method	ANCOVA

	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	2.07
	Confidence Interval	(2-Sided) 95% -0.96 to 5.11
	Estimation Comments	[Not specified]

Statistical Analysis 4 for Change From Baseline in Mean Daytime and Night-time SBP and DBP by Ambulatory Blood Pressure Monitoring

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in mean night-time DBP (Day 28)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.002
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	3.14
	Confidence Interval	(2-Sided) 95% 1.13 to 5.14
	Estimation Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Change From Baseline in Mean Awake SBP and DBP by Ambulatory Blood Pressure Monitoring
Measure Description	ANCOVA=analysis of covariance, BID=twice daily, DBP=diastolic blood pressure, FAS=full analysis set, IP=investigational product, SBP=systolic blood pressure.
Time Frame	4 weeks
Safety Issue?	Yes

Analysis Population Description

The FAS includes those randomised patients who received at least 1 dose of IP. Patients were analysed by randomised treatment in accordance with the intention to treat principle.The analysis population for each endpoint includes patients from the FAS still on IP at 4 weeks and with a valid measurement for this type of blood pressure assessment.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment
PLACEBO	Oral treatment

Measured Values

	FOSTA 100 MG BID	PLACEBO
Number of Participants Analyzed	63	62
Change From Baseline in Mean Awake SBP and DBP by Ambulatory Blood Pressure Monitoring [units: mmHg] Mean (Standard Deviation)		
Day 28 awake SBP	4.8 (8.24)	1.4 (8.37)
Day 28 awake DBP	4.8 (4.80)	0.8 (4.69)

Statistical Analysis 1 for Change From Baseline in Mean Awake SBP and DBP by Ambulatory Blood Pressure Monitoring

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in mean awake SBP (Day 28)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.024
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	3.11
	Confidence Interval	(2-Sided) 95% 0.41 to 5.81
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Change From Baseline in Mean Awake SBP and DBP by Ambulatory Blood Pressure Monitoring

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in mean awake DBP (Day 28)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	3.66
	Confidence Interval	(2-Sided) 95% 2.10 to 5.22
	Estimation Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in Mean Sleeping SBP and DBP by Ambulatory Blood Pressure Monitoring
Measure Description	ANCOVA=analysis of covariance, BID=twice daily, DBP=diastolic blood pressure, FAS=full analysis set, IP=investigational product, SBP=systolic blood pressure.
Time Frame	4 weeks
Safety Issue?	Yes

Analysis Population Description

The FAS includes those randomised patients who received at least 1 dose of IP. Patients were analysed by randomised treatment in accordance with the intention to treat principle.The analysis population for each endpoint includes patients from the FAS still on IP at 4 weeks and with a valid measurement for this type of blood pressure assessment.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment
PLACEBO	Oral treatment

Measured Values

	FOSTA 100 MG BID	PLACEBO
Number of Participants Analyzed	58	60
Change From Baseline in Mean Sleeping SBP and DBP by Ambulatory Blood Pressure Monitoring [units: mmHg] Mean (Standard Deviation)		
Day 28 sleeping SBP	2.4 (8.86)	0.7 (10.12)
Day 28 sleeping DBP	2.8 (6.28)	0.5 (6.72)

Statistical Analysis 1 for Change From Baseline in Mean Sleeping SBP and DBP by Ambulatory Blood Pressure Monitoring

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in mean sleeping SBP
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.223
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least squares mean treatment difference]

	Estimated Value	1.99
	Confidence Interval	(2-Sided) 95% -1.22 to 5.20
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Change From Baseline in Mean Sleeping SBP and DBP by Ambulatory Blood Pressure Monitoring

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in mean sleeping DBP
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.007
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	2.87
	Confidence Interval	(2-Sided) 95% 0.81 to 4.93
	Estimation Comments	[Not specified]

6. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in Clinic SBP and DBP
Measure Description	Blood pressure was measured in the clinic using an automated blood pressure machine (oscillometric method). Three separate measurements were taken 2 to 5 minutes apart and the mean of the 2nd and 3rd measurements calculated. ANCOVA=analysis of covariance, BID=twice daily, DBP=diastolic blood pressure, FAS=full analysis set, IP=investigational product, SBP=systolic blood pressure.
Time Frame	4 weeks
Safety Issue?	Yes

Analysis Population Description

The FAS includes those randomised patients who received at least 1 dose of IP. Patients were analysed by randomised treatment in accordance with the intention to treat principle.The analysis population for each endpoint includes patients from the FAS still on IP at 4 weeks and with a valid measurement for this type of blood pressure assessment.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment
PLACEBO	Oral treatment

Measured Values

	FOSTA 100 MG BID	PLACEBO
Number of Participants Analyzed	64	64
Mean Change From Baseline in Clinic SBP and DBP [units: mmHg] Mean (Standard Deviation)		
Day 29 SBP	3.8 (11.53)	2.9 (9.61)
Day 29 DBP	2.7 (7.88)	0.7 (6.72)

Statistical Analysis 1 for Mean Change From Baseline in Clinic SBP and DBP

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in clinic SBP (Day 29)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.200
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	2.24

	Confidence Interval	(2-Sided) 95% -1.20 to 5.69
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Mean Change From Baseline in Clinic SBP and DBP

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in clinic DBP (Day 29)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.046
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	2.36
	Confidence Interval	(2-Sided) 95% 0.05 to 4.68
	Estimation Comments	[Not specified]

7. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in Morning Pre-dose Home SBP and DBP
Measure Description	ANCOVA=analysis of covariance, BID=twice daily, DBP=diastolic blood pressure, FAS=full analysis set, IP=investigational product, SBP=systolic blood pressure.
Time Frame	4 weeks
Safety Issue?	Yes

Analysis Population Description

The FAS includes those randomised patients who received at least 1 dose of IP. Patients were analysed by randomised treatment in accordance with the intention to treat principle.The analysis population for each endpoint includes patients from the FAS still on IP at 4 weeks and with a valid measurement for this type of blood pressure assessment.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment
PLACEBO	Oral treatment

Measured Values

	FOSTA 100 MG BID	PLACEBO
Number of Participants Analyzed	62	59
Mean Change From Baseline in Morning Pre-dose Home SBP and DBP [units: mmHg] Mean (Standard Deviation)		
Weekly average pre-dose SBP (Week 4)	5.1 (8.53)	-1.3 (6.50)
Weekly average pre-dose DBP (Week 4)	4.0 (5.82)	-0.4 (3.78)

Statistical Analysis 1 for Mean Change From Baseline in Morning Pre-dose Home SBP and DBP

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in weekly average pre-dose home SBP (Week 4)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	6.31
	Confidence Interval	(2-Sided) 95% 3.60 to 9.03
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Mean Change From Baseline in Morning Pre-dose Home SBP and DBP

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in weekly average pre-dose home DBP (Week 4)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	4.58
	Confidence Interval	(2-Sided) 95% 2.91 to 6.25
	Estimation Comments	[Not specified]

8. Secondary Outcome Measure:

Measure Title	Mean Change From Baseline in Evening Post-dose Home SBP and DBP
Measure Description	ANCOVA=analysis of covariance, BID=twice daily, DBP=diastolic blood pressure, FAS=full analysis set, IP=investigational product, SBP=systolic blood pressure.
Time Frame	4 weeks
Safety Issue?	Yes

Analysis Population Description

The FAS includes those randomised patients who received at least 1 dose of IP. Patients were analysed by randomised treatment in accordance with the intention to treat principle.The analysis population for each endpoint includes patients from the FAS still on IP at 4 weeks and with a valid measurement for this type of blood pressure assessment.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment

	Description
PLACEBO	Oral treatment

Measured Values

	FOSTA 100 MG BID	PLACEBO
Number of Participants Analyzed	61	59
Mean Change From Baseline in Evening Post-dose Home SBP and DBP [units: mmHg] Mean (Standard Deviation)		
Weekly average post-dose SBP (Week 4)	5.3 (9.11)	-1.6 (7.71)
Weekly average post-dose DBP (Week 4)	3.7 (5.69)	-1.0 (4.95)

Statistical Analysis 1 for Mean Change From Baseline in Evening Post-dose Home SBP and DBP

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in weekly average post-dose home SBP (Week 4)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)
Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	7.22
	Confidence Interval	(2-Sided) 95% 4.29 to 10.16
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Mean Change From Baseline in Evening Post-dose Home SBP and DBP

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Change from baseline in weekly average post-dose home DBP (Week 4)
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	ANCOVA
	Comments	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)
Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	4.74
	Confidence Interval	(2-Sided) 95% 2.90 to 6.59
	Estimation Comments	[Not specified]

9. Secondary Outcome Measure:

Measure Title	Mean Change From Completion/Discontinuation to Follow-up in Clinical Measurement of SBP and DBP
Measure Description	BID=twice daily, DBP=diastolic blood pressure, FAS=full analysis set, IP=investigational product, SBP=systolic blood pressure.
Time Frame	Day 29 to Day 36
Safety Issue?	Yes

Analysis Population Description

The FAS includes those randomised patients who received at least 1 dose of IP. Patients were analysed by randomised treatment in accordance with the intention to treat principle. The analysis population for each endpoint includes patients from the FAS still on IP at Day 36 and with a valid measurement for this type of blood pressure assessment.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment

	Description
PLACEBO	Oral treatment

Measured Values

	FOSTA 100 MG BID	PLACEBO
Number of Participants Analyzed	64	64
Mean Change From Completion/Discontinuation to Follow-up in Clinical Measurement of SBP and DBP [units: mmHg] Mean (Standard Deviation)		
SBP	-3.3 (12.32)	-0.5 (9.25)
DBP	-1.8 (9.56)	-0.6 (6.38)

10. Secondary Outcome Measure:

Measure Title	DAS28-CRP Improvement
Measure Description	ANCOVA=analysis of covariance, BID=twice daily, DAS28-CRP=Disease Activity Score based on a count of swollen and tender joints (out of 28 joints), blood test measures of inflammation (C-reactive protein [CRP]) and the patient's own assessment, FAS=full analysis set, IP=investigational product. Scores can take any positive value with a lower value indicative of a better clinical condition. Mean changes from baseline in DAS28-CRP score are shown at each visit and are presented as decreases from baseline (defined as baseline minus post-baseline) with larger changes indicating a better clinical condition.
Time Frame	4 weeks
Safety Issue?	No

Analysis Population Description

The FAS includes those randomised patients who received at least 1 dose of IP. Patients were analysed by randomised treatment in accordance with the intention to treat principle. The analysis population for each endpoint includes those patients from the FAS who were still on IP at 4 weeks and had a valid measurement for this type of assessment.

Reporting Groups

	Description
FOSTA 100 MG BID	Fostamatinib 100 mg bid, oral treatment
PLACEBO	Oral treatment

Measured Values

	FOSTA 100 MG BID	PLACEBO
Number of Participants Analyzed	67	67
DAS28-CRP Improvement [units: Units on a scale] Mean (Standard Deviation)		
Day 8	0.8 (0.77)	0.3 (0.61)
Day 15	1.0 (1.06)	0.3 (0.77)
Day 29	1.2 (1.06)	0.5 (1.00)

Statistical Analysis 1 for DAS28-CRP Improvement

Statistical Analysis Overview	Comparison Groups	FOSTA 100 MG BID, PLACEBO
	Comments	Improvement from baseline at Day 29. Non-responder imputation has been applied following premature withdrawal, or any dose of background disease modifying antirheumatic drug increased or any other RA treatment initiated including DMARDs, anti-TNFs or other biologics, or receiving 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	Inc. baseline (covariate); treatment, region, prior failure to biologic disease modifying antirheumatic drug & baseline antihypertensive use (factors)
	Method	ANCOVA
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Least square means treatment difference]
	Estimated Value	0.74
	Confidence Interval	(2-Sided) 95% 0.40 to 1.08
	Estimation Comments	[Not specified]

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
FOSTA 100 MG BID	
PLACEBO	

Serious Adverse Events

	FOSTA 100 MG BID		PLACEBO	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	0/68 (0%)		0/67 (0%)	

Other Adverse Events

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

	FOSTA 100 MG BID		PLACEBO	
	Affected/At Risk (%)	# Events	Affected/At Risk (%)	# Events
Total	2/68 (2.94%)		4/67 (5.97%)	
Gastrointestinal disorders				
DIARRHOEA [A] †	2/68 (2.94%)	3	4/67 (5.97%)	4

† 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 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.

The disclosure restriction on the PI is that the sponsor can review and comment on results communications prior to publication or presentation. Sponsor will be allowed a review period of at least 60 days from submission but can request that the submission be delayed for an additional 90 days from the date of Sponsor's request.

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