



Clinical trial results:

Randomized, Parallel, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of SBI-087 in Seropositive Subjects With Active Rheumatoid Arthritis on a Stable Background of Methotrexate

Summary

EudraCT number	2009-010516-15
Trial protocol	HU ES PL GR
Global end of trial date	25 July 2013

Results information

Result version number	v1 (current)
This version publication date	23 May 2016
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	3227K1-2000
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01008852
WHO universal trial number (UTN)	-
Other trial identifiers	Alias: B2261003

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 July 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 July 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate clinical efficacy and safety of 4 SBI-087 subcutaneous (SC) dosing regimens versus placebo in seropositive subjects with active rheumatoid arthritis (RA) on a stable background of Methotrexate (MTX).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 December 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Chile: 6
Country: Number of subjects enrolled	Japan: 36
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Serbia: 37
Country: Number of subjects enrolled	United States: 64
Country: Number of subjects enrolled	Poland: 35
Country: Number of subjects enrolled	Spain: 9
Worldwide total number of subjects	209
EEA total number of subjects	55

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	169
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 210 subjects in 10 countries were enrolled in this study. Out of these 210 subjects, 209 subjects received the study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SBI-087/ Placebo/ Placebo

Arm description:

Subjects with active RA and on a on a stable background of MTX, received SBI-087 on Day 1 and placebo matched to SBI-087 on Day 15 and 84 during the initial phase of study. Subjects were followed up after day 168 of initial phase up to 2 years.

Arm type	Experimental
Investigational medicinal product name	SBI-087
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 200 milligram (mg) SBI-087 SC injection on Day 1.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received placebo matched to SBI-087 on Day 15 and 84.

Arm title	SBI-087/ SBI-087/ Placebo
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Arm description:

Subjects with active RA on a stable background of MTX, received SBI-087 on Day 1, 15 and placebo matched to SBI-087 on Day 84. Subjects were followed up after day 168 of initial phase up to 2 years.

Arm type	Experimental
Investigational medicinal product name	SBI-087
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 200 mg SBI-087 SC injection on Day 1 and Day 15.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Subjects received placebo matched to SBI-087 on Day 84.	
Arm title	SBI-087/ Placebo/ SBI-087

Arm description:

Subjects with active RA on a stable background of MTX, received SBI-087 200 mg on Day 1, 84 and placebo matched to SBI-087 on Day 15. Subjects were followed up after day 168 of initial phase up to 2 years.

Arm type	Experimental
Investigational medicinal product name	SBI-087
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 200 mg SBI-087 SC injection on Day 1 and Day 84.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received placebo matched to SBI-087 on Day 15.

Arm title	SBI-087/ SBI-087/ SBI-087
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Arm description:

Subjects with active RA on a stable background of MTX, received SBI-087 200 mg on Day 1, 15 and 84. Subjects were followed up after day 168 of initial phase up to 2 years.

Arm type	Experimental
Investigational medicinal product name	SBI-087
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 200 mg SBI-087 SC injection on Day 1, 15 and 84.

Arm title	Placebo/ Placebo/ Placebo
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Arm description:

Subjects with active RA on a stable background of MTX, received placebo matched to SBI-087 on Day 1, 15 and 84. Subjects were followed up after day 168 of initial phase up to 2 years.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received placebo matched to SBI-087 SC injection on Day 1, 15 and 84.

Number of subjects in period 1	SBI-087/ Placebo/ Placebo	SBI-087/ SBI-087/ Placebo	SBI-087/ Placebo/ SBI-087
Started	43	42	43
Initial Phase	34	36	32
Completed	20	29	21
Not completed	23	13	22
Consent withdrawn by subject	10	5	10
Physician decision	1	2	1
Adverse Event	4	2	3
Death	-	1	2
Protocol Violation	2	1	1
Lost to follow-up	1	-	1
Lack of efficacy	5	2	4

Number of subjects in period 1	SBI-087/ SBI-087/ SBI-087	Placebo/ Placebo/ Placebo
Started	41	40
Initial Phase	37	33
Completed	26	26
Not completed	15	14
Consent withdrawn by subject	10	2
Physician decision	-	2
Adverse Event	-	2
Death	-	-
Protocol Violation	-	-
Lost to follow-up	-	1
Lack of efficacy	5	7

Baseline characteristics

Reporting groups

Reporting group title	SBI-087/ Placebo/ Placebo
Reporting group description:	
Subjects with active RA and on a on a stable background of MTX, received SBI-087 on Day 1 and placebo matched to SBI-087 on Day 15 and 84 during the initial phase of study. Subjects were followed up after day 168 of initial phase up to 2 years.	
Reporting group title	SBI-087/ SBI-087/ Placebo
Reporting group description:	
Subjects with active RA on a stable background of MTX, received SBI-087 on Day 1, 15 and placebo matched to SBI-087 on Day 84. Subjects were followed up after day 168 of initial phase up to 2 years.	
Reporting group title	SBI-087/ Placebo/ SBI-087
Reporting group description:	
Subjects with active RA on a stable background of MTX, received SBI-087 200 mg on Day 1, 84 and placebo matched to SBI-087 on Day 15. Subjects were followed up after day 168 of initial phase up to 2 years.	
Reporting group title	SBI-087/ SBI-087/ SBI-087
Reporting group description:	
Subjects with active RA on a stable background of MTX, received SBI-087 200 mg on Day 1, 15 and 84. Subjects were followed up after day 168 of initial phase up to 2 years.	
Reporting group title	Placebo/ Placebo/ Placebo
Reporting group description:	
Subjects with active RA on a stable background of MTX, received placebo matched to SBI-087 on Day 1, 15 and 84. Subjects were followed up after day 168 of initial phase up to 2 years.	

Reporting group values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI-087/ Placebo	SBI-087/ Placebo/ SBI-087
Number of subjects	43	42	43
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	56.77	53.86	52.88
standard deviation	± 10.79	± 10.83	± 14.22
Gender categorical			
Units: Subjects			
Female	35	30	34
Male	8	12	9

Reporting group values	SBI-087/ SBI-087/ SBI-087	Placebo/ Placebo/ Placebo	Total
Number of subjects	41	40	209
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	57.93	52.03	
standard deviation	± 10.62	± 13.58	-

Gender categorical			
Units: Subjects			
Female	32	33	164
Male	9	7	45

End points

End points reporting groups

Reporting group title	SBI-087/ Placebo/ Placebo
Reporting group description: Subjects with active RA and on a on a stable background of MTX, received SBI-087 on Day 1 and placebo matched to SBI-087 on Day 15 and 84 during the initial phase of study. Subjects were followed up after day 168 of initial phase up to 2 years.	
Reporting group title	SBI-087/ SBI-087/ Placebo
Reporting group description: Subjects with active RA on a stable background of MTX, received SBI-087 on Day 1, 15 and placebo matched to SBI-087 on Day 84. Subjects were followed up after day 168 of initial phase up to 2 years.	
Reporting group title	SBI-087/ Placebo/ SBI-087
Reporting group description: Subjects with active RA on a stable background of MTX, received SBI-087 200 mg on Day 1, 84 and placebo matched to SBI-087 on Day 15. Subjects were followed up after day 168 of initial phase up to 2 years.	
Reporting group title	SBI-087/ SBI-087/ SBI-087
Reporting group description: Subjects with active RA on a stable background of MTX, received SBI-087 200 mg on Day 1, 15 and 84. Subjects were followed up after day 168 of initial phase up to 2 years.	
Reporting group title	Placebo/ Placebo/ Placebo
Reporting group description: Subjects with active RA on a stable background of MTX, received placebo matched to SBI-087 on Day 1, 15 and 84. Subjects were followed up after day 168 of initial phase up to 2 years.	

Primary: Percentage of Subjects Achieving American College of Rheumatology 20% (ACR20) Response at Week 16

End point title	Percentage of Subjects Achieving American College of Rheumatology 20% (ACR20) Response at Week 16 ^[1]
End point description: ACR20 response: greater than or equal to ($\geq$) 20 percent (%) improvement in tender joints count with 28 joints (TJC28); $\geq$ 20% improvement in swollen joints count with 28 joints (SJC28); and $\geq$ 20% improvement in at least 3 of 5 remaining ACR core measures: subject assessment of pain; subject global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the Health Assessment Questionnaire [HAQ]); and C-Reactive Protein (CRP). Modified intent-to-treat (mITT) population included all randomized subjects who received any portion of investigational product. Missing values were imputed using the last observation carried forward (LOCF).	
End point type	Primary
End point timeframe: Week 16	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis has been provided separately as an attachment.

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: Percentage of subjects				
number (not applicable)	55.81	54.76	51.16	70.73

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Percentage of subjects				
number (not applicable)	50			

Attachments (see zip file)	ACR20: SBI-087/ Placebo/ Placebo /20150708_3227K1-2000
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Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Swollen Joints Count (SJC) at Week 2, 4,8, 12, 16,20, 24

End point title	Change from Baseline in Swollen Joints Count (SJC) at Week 2, 4,8, 12, 16,20, 24
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End point description:

Number of swollen joints was determined by examination of 28 joints and identifying when swelling was present. The number of swollen joints was recorded on the joint assessment form at each visit, no swelling = 0, swelling =1. A negative value in change from baseline indicates an improvement. Least square mean and standard error are estimated from an analysis of covariance (ANCOVA) model with treatment, prior anti-tumor necrosis factor (TNF) failure and geographic region as covariates. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, 4, 8, 12, 16, 20, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: joints				
least squares mean (standard error)				
Baseline	11.42 (± 4.62)	10.53 (± 4.83)	11.87 (± 6.04)	10.38 (± 5.22)
Change at Week 2	-3.03 (± 0.63)	-2.42 (± 0.63)	-2.42 (± 0.63)	-3.09 (± 0.64)
Change at Week 4	-5.12 (± 0.63)	-5.37 (± 0.63)	-3.75 (± 0.63)	-5.77 (± 0.63)
Change at Week 8	-6.05 (± 0.67)	-5.56 (± 0.67)	-4.78 (± 0.67)	-5.83 (± 0.68)
Change at Week 12	-6.27 (± 0.65)	-5.69 (± 0.64)	-5.05 (± 0.64)	-6.42 (± 0.65)
Change at Week 16	-5.67 (± 0.69)	-5.69 (± 0.69)	-5.22 (± 0.69)	-6.95 (± 0.7)
Change at Week 20	-6.74 (± 0.68)	-6.72 (± 0.67)	-5.24 (± 0.67)	-7.48 (± 0.68)
Change at Week 24	-5.58 (± 0.74)	-7.16 (± 0.74)	-5.74 (± 0.74)	-7.64 (± 0.75)

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: joints				
least squares mean (standard error)				
Baseline	10.41 (± 5.34)			
Change at Week 2	-3.13 (± 0.64)			
Change at Week 4	-4.91 (± 0.64)			
Change at Week 8	-4.74 (± 0.69)			
Change at Week 12	-4.5 (± 0.66)			
Change at Week 16	-5.87 (± 0.7)			
Change at Week 20	-5.75 (± 0.69)			
Change at Week 24	-6.37 (± 0.75)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Tender Joints Count (TJC) at Week 2, 4, 8, 12, 16, 20, 24

End point title	Change From Baseline in Tender Joints Count (TJC) at Week 2, 4, 8, 12, 16, 20, 24
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End point description:

Number of tender joints was determined by examining 28 joints and identified the joints that were painful under pressure or to passive motion. The number of tender joints was recorded on the joint assessment form at each visit, no tenderness = 0, tenderness = 1. A negative value in change from baseline indicates an improvement. Least square mean and standard error are estimated from an ANCOVA model with treatment, prior anti-TNF failure and geographic region as covariates. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, 4, 8, 12, 16, 20, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: joints				
least squares mean (standard error)				
Baseline	15.1 (± 6.32)	13.02 (± 6.04)	14.17 (± 5.88)	13.39 (± 6.37)
Change at Week 2	-3.47 (± 0.76)	-2.66 (± 0.76)	-2.19 (± 0.76)	-3.01 (± 0.77)
Change at Week 4	-5.85 (± 0.85)	-6.94 (± 0.84)	-3.96 (± 0.84)	-6.08 (± 0.85)

Change at Week 8	-6.32 (± 0.9)	-7.55 (± 0.9)	-5.75 (± 0.89)	-7.61 (± 0.91)
Change at Week 12	-7.06 (± 0.9)	-7.67 (± 0.9)	-5.89 (± 0.9)	-7.38 (± 0.91)
Change at Week 16	-7.39 (± 0.92)	-7.9 (± 0.91)	-6.13 (± 0.91)	-8.08 (± 0.92)
Change at Week 20	-7.48 (± 0.94)	-7.73 (± 0.94)	-6.04 (± 0.63)	-9.01 (± 0.95)
Change at Week 24	-6.38 (± 0.95)	-7.88 (± 0.95)	-7.06 (± 0.96)	-9.61 (± 0.956)

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: joints				
least squares mean (standard error)				
Baseline	13.43 (± 7.34)			
Change at Week 2	-3.43 (± 0.78)			
Change at Week 4	-4.98 (± 0.86)			
Change at Week 8	-5.43 (± 0.92)			
Change at Week 12	-4.65 (± 0.92)			
Change at Week 16	-6.79 (± 0.93)			
Change at Week 20	-5.26 (± 0.96)			
Change at Week 24	-6.07 (± 0.97)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving American College of Rheumatology 20% (ACR20) Response at Week 2, 8, 12 and 24

End point title	Percentage of Subjects Achieving American College of Rheumatology 20% (ACR20) Response at Week 2, 8, 12 and 24
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End point description:

ACR20 response: greater than or equal to ($\geq$) 20 percent (%) improvement in tender joints count (TJC); $\geq$ 20% improvement in swollen joints count (SJC); and $\geq$ 20% improvement in at least 3 of 5 remaining ACR core measures: subject assessment of pain; subject global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the Health Assessment Questionnaire [HAQ]); and C-Reactive Protein (CRP). mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF. Here 'n' signifies subjects who were evaluable at specified time points for each arm group, respectively.

End point type	Secondary
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End point timeframe:

Week 2, 8, 12, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: Percentage of subjects				
number (not applicable)				
Week 2 (n=43, 42, 43, 41, 40)	18.6	14.29	13.95	14.63
Week 8 (n=43, 42, 43, 41, 40)	48.84	52.38	41.86	56.1
Week 12 (n=43, 41, 43, 41, 40)	53.49	53.66	44.19	58.54
Week 24 (n=43, 42, 43, 41, 40)	55.81	54.76	60.47	70.73

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Percentage of subjects				
number (not applicable)				
Week 2 (n=43, 42, 43, 41, 40)	12.5			
Week 8 (n=43, 42, 43, 41, 40)	30			
Week 12 (n=43, 41, 43, 41, 40)	42.5			
Week 24 (n=43, 42, 43, 41, 40)	50			

Attachments (see zip file)	ACR20 Week 2: SBI-087/ Placebo/ Placebo
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving American College of Rheumatology 50% (ACR50) Response at Week 2, 8, 12, 16 and 24

End point title	Percentage of Subjects Achieving American College of Rheumatology 50% (ACR50) Response at Week 2, 8, 12, 16 and 24
End point description:	ACR50 response: ≥ 50 percent (%) improvement in TJC; $\geq 50\%$ improvement in SJC; and $\geq 50\%$ improvement in at least 3 of 5 remaining ACR core measures: subject assessment of pain; subject global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the HAQ); and CRP. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF.
End point type	Secondary
End point timeframe:	
Week 2, 8, 12, 16, 24	

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: Percentage of subjects				
number (not applicable)				
Week 2	4.65	0	2.33	2.44
Week 8	18.6	14.29	25.58	29.27
Week 12	20.93	33.33	23.26	17.07
Week 16	23.26	33.33	23.26	39.02
Week 24	27.91	38.1	34.88	43.9

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Percentage of subjects				
number (not applicable)				
Week 2	5			
Week 8	20			
Week 12	7.5			
Week 16	25.64			
Week 24	30			

Attachments (see zip file)	ACR50 Week 2: SBI-087/ Placebo/ Placebo
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving American College of Rheumatology 70% (ACR70) Response at Week 2, 8, 12, 16 and 24

End point title	Percentage of Subjects Achieving American College of Rheumatology 70% (ACR70) Response at Week 2, 8, 12, 16 and 24
End point description: ACR70 response: $\geq 70\%$ improvement in TJC; $\geq 70\%$ improvement in SJC; and $\geq 70\%$ improvement in at least 3 of 5 remaining ACR core measures: subject assessment of pain; subject global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the HAQ); and CRP. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF.	
End point type	Secondary
End point timeframe: Week 2, 8, 12, 16, 24	

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: Percentage of subjects				
number (not applicable)				
Week 2	0	0	0	0
Week 8	9.3	0	4.65	2.44
Week 12	6.98	2.38	2.33	7.32
Week 16	6.98	11.9	16.28	12.2
Week 24	11.63	11.9	20.93	24.39

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Percentage of subjects				
number (not applicable)				
Week 2	0			
Week 8	10			
Week 12	2.5			
Week 16	7.5			
Week 24	5			

Attachments (see zip file)	ACR70 Week 2: SBI-087/ Placebo/ Placebo/20150708_3227K1-
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Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Hybrid Measure of American College of Rheumatology (ACR)

End point title	Percentage of Subjects With Hybrid Measure of American College of Rheumatology (ACR)
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End point description:

Average percentage improvement in ACR core set measures of subjects were calculated. If a core set measure worsened by 100%, that percentage improvement was limited to --100%. This measure was used to determine whether subject had achieved: ACR20, 50, or 70. ACR20, 50 or 70 responses: ≥ 20 or 50 or 70% (respective) improvement in tender joint count or in swollen joint count; and ≥ 20 or 50 or 70% (respective) improvement in at least 3 of 5 remaining ACR core measures: subject assessment of pain; subject global assessment of disease activity; physician global assessment of disease activity; self-assessed disability (disability index of the HAQ); and CRP. A table was used to obtain the Hybrid ACR response measure, where, ACR status of the subject (left column) and the mean percentage improvement in core set items was taken, the Hybrid ACR score is where they intersect in the table.

End point type	Secondary
End point timeframe:	
Week 2, 8, 12, 16, 24	

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[2]	0 ^[3]	0 ^[4]	0 ^[5]
Units: Percentage of subjects				
number (not applicable)				

Notes:

[2] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[3] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[4] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[5] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[6]			
Units: Percentage of subjects				
number (not applicable)				

Notes:

[6] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Secondary: American College of Rheumatology Numeric Response (ACR-N)

End point title	American College of Rheumatology Numeric Response (ACR-N)
End point description:	
ACR--N was calculated by taking the (1) lowest percentage improvement in swollen joint count or (2) lowest percentage improvement in tender joint count or (3) the median of the remaining 5 components of the ACR response (subject's assessment of disease activity; subject's global assessment of pain; physician's assessment of disease activity; subject's assessment of physical function; an acute phase reactant value -C-reactive protein [CRP]). Negative numbers indicate worsening.	
End point type	Secondary
End point timeframe:	
Week 2, 8, 12, 16, 24	

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[7]	0 ^[8]	0 ^[9]	0 ^[10]
Units: Units on scale				
number (not applicable)				

Notes:

[7] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[8] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[9] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[10] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[11]			
Units: Units on scale				
number (not applicable)				

Notes:

[11] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Numeric Index of American College of Rheumatology Response (ACR--n) Curve

End point title	Area Under the Numeric Index of American College of Rheumatology Response (ACR--n) Curve
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End point description:

ACR-n: calculated by taking the (1) lowest percentage improvement in swollen joint count or (2) lowest percentage improvement in tender joint count or (3) the median of the remaining 5 components of the ACR response (subject's assessment of disease activity; subject's global assessment of pain; physician's assessment of disease activity; subject's assessment of physical function; an acute phase reactant value -C-reactive protein [CRP]). Negative numbers indicate worsening. The area under the curve (AUC) for ACR--n is the measure of the AUC of the mean change from baseline in ACR--n.

End point type	Secondary
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End point timeframe:

Baseline up to Week 16, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[12]	0 ^[13]	0 ^[14]	0 ^[15]
Units: Units on scale*weeks				
number (not applicable)				

Notes:

[12] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[13] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[14] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[15] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[16]			
Units: Units on scale*weeks				
number (not applicable)				

Notes:

[16] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in C--Reactive Protein (CRP) at Week 2, 8, 12, 16, 24

End point title	Change From Baseline in C--Reactive Protein (CRP) at Week 2, 8, 12, 16, 24
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End point description:

The test for CRP is a laboratory measurement for evaluation of an acute phase reactant of inflammation through the use of an ultrasensitive assay. Normal range of CRP is 0 milligram per liter (mg/L) to 100 mg/L. A decrease in the level of CRP indicates reduction in inflammation and therefore improvement. Least square mean and standard error are estimated from an ANCOVA model with treatment, prior anti-TNF failure and geographic region as covariates. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, 8, 12, 16, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: milligram per deciliter (mg/dL)				
least squares mean (standard error)				
Baseline	15.89 (± 16.22)	15.78 (± 20.23)	22.23 (± 22.36)	14.13 (± 16.26)
Change at Week 2	-1.19 (± 1.91)	-1.28 (± 1.9)	-0.25 (± 1.91)	0.53 (± 1.93)
Change at Week 8	-5.86 (± 2.83)	-1.97 (± 2.83)	-0.25 (± 2.84)	-4.1 (± 2.86)
Change at Week 12	-7.48 (± 2.13)	-7.9 (± 2.13)	-4.48 (± 2.14)	-8.83 (± 2.16)
Change at Week 16	-7.71 (± 2.06)	-8.44 (± 2.06)	-5.25 (± 2.07)	-9.17 (± 2.09)
Change at Week 24	-6.81 (± 2.38)	-6.56 (± 2.37)	-6.07 (± 2.38)	-8.78 (± 2.4)

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: milligram per deciliter (mg/dL)				
least squares mean (standard error)				
Baseline	21.79 ($\pm$ 34)			
Change at Week 2	0.09 ($\pm$ 1.96)			
Change at Week 8	-1.89 ($\pm$ 2.91)			
Change at Week 12	1.17 ($\pm$ 2.19)			
Change at Week 16	-1.51 ($\pm$ 2.12)			
Change at Week 24	-0.77 ($\pm$ 2.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Pain Using Visual Analogue Scale (VAS) at Week 2, 4, 8, 12, 16, 20, 24

End point title	Change From Baseline in Pain Using Visual Analogue Scale (VAS) at Week 2, 4, 8, 12, 16, 20, 24
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End point description:

VAS consists of a line 0 to 100 millimeters (mm) in length; range is (no pain) to 100 mm (worst possible pain). Subjects placed a mark indicating the intensity of their pain. Higher score indicates greater level of pain. Change = observation minus baseline. Least square mean and standard error are estimated from an ANCOVA model with treatment, prior anti-TNF failure and geographic region as covariates. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using the LOCF.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, 4, 8, 12, 16, 20, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: mm				
least squares mean (standard error)				
Baseline	49.48 ($\pm$ 21.04)	58.81 ($\pm$ 20.52)	61.42 ($\pm$ 19.11)	54.22 ($\pm$ 21.38)
Change at Week 2	-7.92 ($\pm$ 2.73)	-2.83 ($\pm$ 2.7)	-5.42 ($\pm$ 2.7)	-6.51 ($\pm$ 2.73)
Change at Week 4	-8.43 ($\pm$ 3.06)	-13.86 ($\pm$ 3.02)	-8.82 ($\pm$ 3.02)	-12.23 ($\pm$ 3.06)
Change at Week 8	-12.82 ($\pm$ 3.38)	-10.98 ($\pm$ 3.33)	-10.15 ($\pm$ 3.33)	-19.46 ($\pm$ 3.38)

Change at Week 12	-13.4 (± 3.47)	-12.91 (± 3.43)	-13.18 (± 3.43)	-12.26 (± 3.48)
Change at Week 16	-14.71 (± 3.68)	-15.67 (± 3.63)	-14.55 (± 3.64)	-23.72 (± 3.68)
Change at Week 20	-18.41 (± 3.5)	-14.48 (± 3.46)	-15.95 (± 3.46)	-23.68 (± 3.51)
Change at Week 24	-16.5 (± 3.6)	-15.87 (± 3.55)	-21.59 (± 3.55)	-22.68 (± 3.6)

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: mm				
least squares mean (standard error)				
Baseline	59.33 (± 20)			
Change at Week 2	-1.71 (± 2.76)			
Change at Week 4	-9.33 (± 3.09)			
Change at Week 8	-10.25 (± 3.41)			
Change at Week 12	-9.94 (± 3.51)			
Change at Week 16	-13.05 (± 3.72)			
Change at Week 20	-14.26 (± 3.54)			
Change at Week 24	-15.83 (± 3.63)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Physician Global Assessment (PGA) of Disease Activity at Week 2, 4, 8, 12, 16, 20, 24

End point title	Change From Baseline in Physician Global Assessment (PGA) of Disease Activity at Week 2, 4, 8, 12, 16, 20, 24
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End point description:

Physicians were asked to assess the disease activity of subjects within the past 3 days. Disease activity was evaluated on an 11-point scale: min = 0 (no disease activity), max = 10 (extreme disease activity). Least square mean and standard error are estimated from an ANCOVA model with treatment, prior anti-TNF failure and geographic region as covariates. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, 4, 8, 12, 16, 20, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: Units on scale				
least squares mean (standard error)				
Baseline	6.4 (± 1.61)	6.69 (± 1.57)	6.67 (± 1.46)	6.41 (± 1.38)
Change at Week 2	-1.59 (± 0.28)	-1.34 (± 0.28)	-0.7 (± 0.28)	-0.84 (± 0.29)
Change at Week 4	-2.38 (± 0.31)	-2.47 (± 0.3)	-1.95 (± 0.3)	-2.2 (± 0.3)
Change at Week 8	-2.74 (± 0.32)	-2.62 (± 0.32)	-2.51 (± 0.31)	-2.95 (± 0.32)
Change at Week 12	-2.82 (± 0.31)	-2.92 (± 0.31)	-2.35 (± 0.32)	-2.76 (± 0.31)
Change at Week 16	-2.77 (± 0.34)	-2.9 (± 0.34)	-2.64 (± 0.33)	-3.32 (± 0.34)
Change at Week 20	-3.21 (± 0.37)	-3.13 (± 0.35)	-3.03 (± 0.37)	-3.45 (± 0.34)
Change at Week 24	-2.82 (± 0.36)	-3.28 (± 0.36)	-2.64 (± 0.36)	-3.67 (± 0.37)

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Units on scale				
least squares mean (standard error)				
Baseline	6.53 (± 1.96)			
Change at Week 2	-1.5 (± 0.29)			
Change at Week 4	-1.83 (± 0.3)			
Change at Week 8	-2.48 (± 0.32)			
Change at Week 12	-2.09 (± 0.31)			
Change at Week 16	-2.51 (± 0.34)			
Change at Week 20	-2.83 (± 0.36)			
Change at Week 24	-2.8 (± 0.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient Global Assessment (PtGA) of Disease Activity at Week 2, 4, 8, 12, 16, 20, 24

End point title	Change From Baseline in Patient Global Assessment (PtGA) of Disease Activity at Week 2, 4, 8, 12, 16, 20, 24
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End point description:

Subjects were asked for the assessment of the overall activity of arthritis. Disease activity was evaluated on an 11-point scale: min = 0 (no disease activity), max = 10 (extreme disease activity). Least square mean and standard error are estimated from an ANCOVA model with treatment, prior anti-TNF failure and geographic region as covariates. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, 4, 8, 12, 16, 20, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: Units on scale				
least squares mean (standard error)				
Baseline	5.93 (± 2.2)	6.4 (± 1.87)	6.72 (± 1.83)	6.59 (± 1.83)
Change at Week 2	-0.83 (± 0.26)	-0.32 (± 0.26)	-0.41 (± 0.26)	-0.86 (± 0.26)
Change at Week 4	-1.2 (± 0.28)	-1.38 (± 0.28)	-1 (± 0.28)	-1.41 (± 0.28)
Change at Week 8	-1.4 (± 0.33)	-1.28 (± 0.33)	-1.2 (± 0.33)	-1.92 (± 0.33)
Change at Week 12	-1.66 (± 0.32)	-1.55 (± 0.32)	-1.35 (± 0.32)	-1.43 (± 0.32)
Change at Week 16	-1.72 (± 0.34)	-1.64 (± 0.34)	-1.44 (± 0.34)	-2.25 (± 0.34)
Change at Week 20	-2.04 (± 0.35)	-1.53 (± 0.34)	-1.79 (± 0.34)	-2.51 (± 0.35)
Change at Week 24	-1.95 (± 0.36)	-1.66 (± 0.36)	-2.17 (± 0.36)	-2.49 (± 0.36)

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Units on scale				
least squares mean (standard error)				
Baseline	6.9 (± 2)			
Change at Week 2	-0.57 (± 0.27)			
Change at Week 4	-1.16 (± 0.29)			
Change at Week 8	-1.3 (± 0.33)			
Change at Week 12	-1.03 (± 0.33)			
Change at Week 16	-1.4 (± 0.35)			
Change at Week 20	-1.61 (± 0.35)			
Change at Week 24	-1.32 (± 0.36)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Duration of Morning Stiffness at Week 2, 4, 8, 12, 16, 20, 24

End point title	Change From Baseline in Duration of Morning Stiffness at Week 2, 4, 8, 12, 16, 20, 24
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End point description:

Duration of morning stiffness is defined as the time elapsed when subject woke up in the morning and was able to resume normal activities without stiffness in minutes. Least square mean and standard error are estimated from an ANCOVA model with treatment, prior anti-TNF failure and geographic region as covariates. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF. Here "99999" in change from baseline in Duration of

morning stiffness signifies not available (NA).

End point type	Secondary
End point timeframe:	
Baseline, Week 2, 4, 8, 12, 16, 20, 24	

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: Minutes				
least squares mean (standard error)				
Baseline	5.93 (± 99999)	6.4 (± 99999)	6.72 (± 99999)	6.59 (± 99999)
Change at Week 2	-46.18 (± 17.03)	-32.26 (± 17.02)	-22.14 (± 17.12)	-27.61 (± 17.22)
Change at Week 4	-45.72 (± 22.75)	-43.58 (± 22.73)	-17.59 (± 22.86)	-45.29 (± 23)
Change at Week 8	-69.88 (± 16.35)	-71.98 (± 16.34)	-76.89 (± 16.43)	-79.87 (± 16.53)
Change at Week 12	-49.27 (± 24.52)	-54.47 (± 24.5)	-16.4 (± 24.64)	-20.64 (± 24.8)
Change at Week 16	-62.82 (± 18.28)	-58.66 (± 18.27)	-23.98 (± 18.37)	-81.56 (± 18.49)
Change at Week 20	-24.34 (± 29.05)	-49 (± 29.03)	-7.6 (± 29.19)	-46.7 (± 29.38)
Change at Week 24	2.74 (± 32.91)	-69.34 (± 32.89)	-49.06 (± 33.07)	-54.02 (± 33.28)

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Minutes				
least squares mean (standard error)				
Baseline	6.9 (± 99999)			
Change at Week 2	-10.58 (± 17.38)			
Change at Week 4	-8.63 (± 23.21)			
Change at Week 8	26.07 (± 16.68)			
Change at Week 12	-5.65 (± 25.02)			
Change at Week 16	-25.26 (± 18.65)			
Change at Week 20	-18.87 (± 29.64)			
Change at Week 24	-24.1 (± 33.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Subjects General Health Visual Analog Scale (VAS) at Week 2, 4, 8, 12, 16, 20, 24

End point title	Change From Baseline in Subjects General Health Visual Analog Scale (VAS) at Week 2, 4, 8, 12, 16, 20, 24
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End point description:

Subjects were simply asked to rate their feelings concerning their arthritis and this assessment was performed more often than prior to administration of study drug. Subjects responded by using a 0 to 100 mm VAS Scale, range is 0 mm (very well) to 100 mm (extremely bad). Change = observation minus baseline. Least square mean and standard error are estimated from an ANCOVA model with treatment, prior anti-TNF failure and geographic region as covariates. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, 4, 8, 12, 16, 20, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: mm				
least squares mean (standard error)				
Baseline	54.72 (± 19.53)	62.1 (± 20)	65.19 (± 17.77)	63.59 (± 17.41)
Change at Week 2	-8.53 (± 2.92)	-4.44 (± 2.88)	-7.61 (± 2.88)	-7.48 (± 2.92)
Change at Week 4	-13.78 (± 2.88)	-13.48 (± 2.83)	-13.09 (± 2.83)	-15.88 (± 2.87)
Change at Week 8	-13.84 (± 3.36)	-10.54 (± 3.31)	-13.04 (± 3.31)	-22.29 (± 3.36)
Change at Week 12	-14.85 (± 3.47)	-15.68 (± 3.41)	-12.51 (± 3.41)	-17.23 (± 3.46)
Change at Week 16	-14.94 (± 3.65)	-16.36 (± 3.59)	-18.03 (± 3.59)	-25.4 (± 3.64)
Change at Week 20	-18.45 (± 3.64)	-15.02 (± 3.59)	-18.48 (± 3.58)	-22.55 (± 3.64)
Change at Week 24	-17.66 (± 3.82)	-16.72 (± 3.76)	-21.4 (± 3.76)	-21.31 (± 3.82)

End point values	Placebo/ Placebo/			
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	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: mm				
least squares mean (standard error)				
Baseline	60.25 (± 22.59)			
Change at Week 2	-4.43 (± 2.95)			
Change at Week 4	-7.84 (± 2.9)			
Change at Week 8	-9.26 (± 3.39)			
Change at Week 12	-7.82 (± 3.49)			
Change at Week 16	-12.03 (± 3.68)			
Change at Week 20	-13.96 (± 3.67)			
Change at Week 24	-11.73 (± 3.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Activity Score Based on 28 Joints Count, General Health Score and C--Reactive Protein (DAS28--4 [CRP]) at Week 2, 8, 12, 16, 24

End point title	Change From Baseline in Disease Activity Score Based on 28 Joints Count, General Health Score and C--Reactive Protein (DAS28--4 [CRP]) at Week 2, 8, 12, 16, 24
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End point description:

DAS28--4 (CRP) was calculated from SJC and TJC using 28 joints count, CRP (mg/dL) and general health score using 100 mm VAS scale. Total score range: 0-9.4, higher score=more disease activity. DAS28--4 (CRP) less than or equal to ($\leq$) 3.2 implied low disease activity and greater than ($>$) 3.2 to 5.1 implied moderate to high disease activity, and DAS28--4 (CRP) less than ($<$) 2.6 = remission. Least square mean and standard error are estimated from an ANCOVA model with treatment, prior anti-TNF failure and geographic region as covariates. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, 8, 12, 16, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: Units on scale				
least squares mean (standard error)				
Baseline	5.65 (± 0.8)	5.52 (± 0.78)	5.83 (± 0.96)	5.51 (± 0.9)
Change at Week 2	-0.66 (± 0.14)	-0.52 (± 0.14)	-0.52 (± 0.14)	-0.62 (± 0.14)
Change at Week 8	-1.41 (± 0.18)	-1.37 (± 0.18)	-1.24 (± 0.18)	-1.68 (± 0.19)
Change at Week 12	-1.5 (± 0.18)	-1.57 (± 0.17)	-1.27 (± 0.18)	-1.67 (± 0.18)

Change at Week 16	-1.63 (± 0.2)	-1.67 (± 0.2)	-1.44 (± 0.2)	-2.05 (± 0.2)
Change at Week 24	-1.54 (± 0.21)	-1.78 (± 0.21)	-1.71 (± 0.21)	-2.14 (± 0.21)

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Units on scale				
least squares mean (standard error)				
Baseline	5.52 (± 1.11)			
Change at Week 2	-0.64 (± 0.14)			
Change at Week 8	-1.19 (± 0.19)			
Change at Week 12	-0.96 (± 0.18)			
Change at Week 16	-1.45 (± 0.2)			
Change at Week 24	-1.34 (± 0.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With European League Against Rheumatism (EULAR) Response Based on DAS28

End point title	Percentage of Subjects With European League Against Rheumatism (EULAR) Response Based on DAS28
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End point description:

The Disease Activity Score Based on 28- joints Count based (DAS28 -based) EULAR response criteria were used to measure individual response as none, good, and moderate, depending on the extent of change from baseline and the level of disease activity reached. Good responders: change from baseline >1.2 with DAS28 ≤ 3.2; moderate responders: change from baseline >1.2 with DAS28 >3.2 or change from baseline >0.6 to ≤1.2 with DAS28 >5.1; non-responders: change from baseline ≤ 0.6 or change from baseline >0.6 and ≤1.2 with DAS28 >5.1.

End point type	Secondary
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End point timeframe:

Week 2, 8, 12, 16, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[17]	0 ^[18]	0 ^[19]	0 ^[20]
Units: Percentage of subjects				
number (not applicable)				

Notes:

[17] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[18] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[19] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

[20] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[21]			
Units: Percentage of subjects				
number (not applicable)				

Notes:

[21] - Data is not reported because analysis was not performed for this endpoint due to Sponsor's decision.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ--DI) at Week 2, 4, 8, 12, 16, 20, 24

End point title	Change From Baseline in Health Assessment Questionnaire Disability Index (HAQ--DI) at Week 2, 4, 8, 12, 16, 20, 24
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End point description:

HAQ--DI: subject-reported assessment of ability to perform tasks in 8 functional categories of daily living activities: dress/groom; arise; eat; walk; reach; grip; hygiene; and common activities over past week. Each item scored on 4--point scale from 0 to 3: 0=no difficulty; 1=some difficulty; 2=much difficulty; 3=unable to do. Overall score was computed as the sum of domain scores and divided by the number of domains answered. Total possible score range 0--3, 0=least functional difficulty and 3=extreme functional difficulty. Change = observation overall score minus baseline overall score. Least square mean and standard error are estimated from an ANCOVA model with treatment, prior anti-TNF failure and geographic region as covariates. mITT population included all randomized subjects who received any portion of investigational product. Missing values were imputed using LOCF.

End point type	Secondary
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End point timeframe:

Baseline, Week 2, 4, 8, 12, 16, 20, 24

End point values	SBI-087/ Placebo/ Placebo	SBI-087/ SBI- 087/ Placebo	SBI-087/ Placebo/ SBI- 087	SBI-087/ SBI- 087/ SBI-087
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	42	43	41
Units: Units on scale				
least squares mean (standard error)				
Baseline	1.46 (± 0.57)	1.46 (± 0.58)	1.54 (± 0.58)	1.36 (± 0.68)
Change at Week 2	-0.16 (± 0.05)	-0.06 (± 0.05)	-0.08 (± 0.05)	-0.1 (± 0.05)
Change at Week 4	-0.16 (± 0.05)	-0.26 (± 0.06)	-0.16 (± 0.06)	-0.29 (± 0.06)
Change at Week 8	-0.22 (± 0.06)	-0.26 (± 0.07)	-0.18 (± 0.07)	-0.3 (± 0.07)
Change at Week 12	-0.21 (± 0.07)	-0.25 (± 0.07)	-0.15 (± 0.07)	-0.34 (± 0.07)
Change at Week 16	-0.36 (± 0.07)	-0.27 (± 0.07)	-0.23 (± 0.07)	-0.43 (± 0.07)
Change at Week 20	-0.32 (± 0.08)	-0.25 (± 0.08)	-0.35 (± 0.09)	-0.42 (± 0.08)
Change at Week 24	-0.3 (± 0.08)	-0.28 (± 0.08)	-0.31 (± 0.08)	-0.44 (± 0.08)

End point values	Placebo/ Placebo/ Placebo			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: Units on scale				
least squares mean (standard error)				
Baseline	1.43 (± 0.8)			
Change at Week 2	-0.17 (± 0.05)			
Change at Week 4	-0.19 (± 0.06)			
Change at Week 8	-0.21 (± 0.07)			
Change at Week 12	-0.28 (± 0.07)			
Change at Week 16	-0.28 (± 0.08)			
Change at Week 20	-0.35 (± 0.08)			
Change at Week 24	-0.24 (± 0.08)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 999 days after last dose of study drug

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as nonserious in another subject, or one subject may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	SBI-087/ Placebo/ Placebo
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Reporting group description:

Subjects with active RA and on a on a stable background of MTX, received SBI-087 on Day 1 and placebo matched to SBI-087 on Day 15 and 84 during the initial phase of study. Subjects were followed up after day 168 of initial phase up to 2 years.

Reporting group title	SBI-087/ SBI-087/ Placebo
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Reporting group description:

Subjects with active RA on a stable background of MTX, received SBI-087 on Day 1, 15 and placebo matched to SBI-087 on Day 84. Subjects were followed up after day 168 of initial phase up to 2 years.

Reporting group title	SBI-087/ Placebo/ SBI-087
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Reporting group description:

Subjects with active RA on a stable background of MTX, received SBI-087 200 mg on Day 1, 84 and placebo matched to SBI-087 on Day 15. Subjects were followed up after day 168 of initial phase up to 2 years.

Reporting group title	SBI-087/ SBI-087/ SBI-087
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Reporting group description:

Subjects with active RA on a stable background of MTX, received SBI-087 200 mg on Day 1, 15 and 84. Subjects were followed up after day 168 of initial phase up to 2 years.

Reporting group title	Placebo/ Placebo/ Placebo
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Reporting group description:

Subjects with active RA on a stable background of MTX, received placebo matched to SBI-087 on Day 1, 15 and 84. Subjects were followed up after day 168 of initial phase up to 2 years.

Serious adverse events	SBI-087/ Placebo/ Placebo	SBI-087/ SBI-087/ Placebo	SBI-087/ Placebo/ SBI-087
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 43 (11.63%)	7 / 42 (16.67%)	7 / 43 (16.28%)
number of deaths (all causes)	0	1	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian neoplasm			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 43 (0.00%)	2 / 42 (4.76%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Respiratory failure			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound decomposition			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Hamartoma			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular encephalopathy			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Visual impairment			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Peptic ulcer			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash generalised			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal colic			

subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 43 (0.00%)	1 / 42 (2.38%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Chronic recurrent multifocal osteomyelitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Rheumatoid arthritis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia necrotising			
subjects affected / exposed	0 / 43 (0.00%)	0 / 42 (0.00%)	1 / 43 (2.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			

subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	SBI-087/ SBI-087/ SBI-087	Placebo/ Placebo/ Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 41 (17.07%)	5 / 40 (12.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian neoplasm			
subjects affected / exposed	1 / 41 (2.44%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Bipolar disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound decomposition			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hamartoma			

subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 41 (2.44%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular encephalopathy			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Leukopenia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Peptic ulcer			
subjects affected / exposed	1 / 41 (2.44%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 41 (2.44%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			

subjects affected / exposed	1 / 41 (2.44%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash generalised			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Chronic recurrent multifocal osteomyelitis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	1 / 41 (2.44%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia necrotising			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	SBI-087/ Placebo/ Placebo	SBI-087/ SBI-087/ Placebo	SBI-087/ Placebo/ SBI-087
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 43 (60.47%)	26 / 42 (61.90%)	29 / 43 (67.44%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 43 (6.98%)	2 / 42 (4.76%)	2 / 43 (4.65%)
occurrences (all)	3	2	7
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 43 (6.98%)	0 / 42 (0.00%)	5 / 43 (11.63%)
occurrences (all)	5	0	6
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 43 (4.65%)	1 / 42 (2.38%)	4 / 43 (9.30%)
occurrences (all)	2	1	6
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	3 / 43 (6.98%)	0 / 42 (0.00%)	7 / 43 (16.28%)
occurrences (all)	5	0	9
General disorders and administration site conditions			

Pyrexia subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	4 / 42 (9.52%) 6	1 / 43 (2.33%) 1
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 2	3 / 42 (7.14%) 4	0 / 43 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2	1 / 42 (2.38%) 1	2 / 43 (4.65%) 2
Diarrhoea subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	2 / 42 (4.76%) 3	1 / 43 (2.33%) 1
Nausea subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 2	1 / 42 (2.38%) 1	4 / 43 (9.30%) 4
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	4 / 42 (9.52%) 4	2 / 43 (4.65%) 2
Skin and subcutaneous tissue disorders			
Dermatitis subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 3	0 / 42 (0.00%) 0	0 / 43 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0	0 / 42 (0.00%) 0	0 / 43 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 5	0 / 42 (0.00%) 0	1 / 43 (2.33%) 1
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1	3 / 42 (7.14%) 3	1 / 43 (2.33%) 1
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	3 / 43 (6.98%)	3 / 42 (7.14%)	2 / 43 (4.65%)
occurrences (all)	4	4	3
Muscle spasms			
subjects affected / exposed	1 / 43 (2.33%)	0 / 42 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Rheumatoid arthritis			
subjects affected / exposed	2 / 43 (4.65%)	2 / 42 (4.76%)	4 / 43 (9.30%)
occurrences (all)	2	2	7
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 43 (9.30%)	1 / 42 (2.38%)	0 / 43 (0.00%)
occurrences (all)	6	3	0
Influenza			
subjects affected / exposed	4 / 43 (9.30%)	2 / 42 (4.76%)	0 / 43 (0.00%)
occurrences (all)	4	2	0
Nasopharyngitis			
subjects affected / exposed	0 / 43 (0.00%)	7 / 42 (16.67%)	2 / 43 (4.65%)
occurrences (all)	0	8	2
Pneumonia			
subjects affected / exposed	0 / 43 (0.00%)	3 / 42 (7.14%)	1 / 43 (2.33%)
occurrences (all)	0	3	1
Upper respiratory tract infection			
subjects affected / exposed	6 / 43 (13.95%)	8 / 42 (19.05%)	10 / 43 (23.26%)
occurrences (all)	8	11	19
Urinary tract infection			
subjects affected / exposed	6 / 43 (13.95%)	2 / 42 (4.76%)	6 / 43 (13.95%)
occurrences (all)	6	3	8

Non-serious adverse events	SBI-087/ SBI-087/ SBI-087	Placebo/ Placebo/ Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 41 (53.66%)	19 / 40 (47.50%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 41 (7.32%)	0 / 40 (0.00%)	
occurrences (all)	4	0	
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	0 / 41 (0.00%) 0	1 / 40 (2.50%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	5 / 41 (12.20%) 13	1 / 40 (2.50%) 3	
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3	0 / 40 (0.00%) 0	
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all)	4 / 41 (9.76%) 4	1 / 40 (2.50%) 1	
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1 3 / 41 (7.32%) 4 4 / 41 (9.76%) 5 2 / 41 (4.88%) 2	0 / 40 (0.00%) 0 0 / 40 (0.00%) 0 4 / 40 (10.00%) 5 1 / 40 (2.50%) 1	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1	2 / 40 (5.00%) 2	
Skin and subcutaneous tissue disorders Dermatitis subjects affected / exposed occurrences (all) Dry skin	0 / 41 (0.00%) 0	1 / 40 (2.50%) 1	

subjects affected / exposed	0 / 41 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	4	
Rash			
subjects affected / exposed	1 / 41 (2.44%)	1 / 40 (2.50%)	
occurrences (all)	1	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 40 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 41 (4.88%)	2 / 40 (5.00%)	
occurrences (all)	2	4	
Muscle spasms			
subjects affected / exposed	0 / 41 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	4	
Rheumatoid arthritis			
subjects affected / exposed	2 / 41 (4.88%)	2 / 40 (5.00%)	
occurrences (all)	2	3	
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 41 (9.76%)	3 / 40 (7.50%)	
occurrences (all)	6	4	
Influenza			
subjects affected / exposed	0 / 41 (0.00%)	2 / 40 (5.00%)	
occurrences (all)	0	2	
Nasopharyngitis			
subjects affected / exposed	4 / 41 (9.76%)	5 / 40 (12.50%)	
occurrences (all)	7	5	
Pneumonia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 40 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 41 (7.32%)	2 / 40 (5.00%)	
occurrences (all)	4	4	
Urinary tract infection			

subjects affected / exposed	3 / 41 (7.32%)	3 / 40 (7.50%)	
occurrences (all)	3	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 October 2009	Clarification of stable doses of methotrexate use throughout the course of the study was added. Documentation of tuberculosis test results were to be available 4 weeks prior to screening visit not baseline visit. Conclusion of Participation eCRF for subjects entering the Follow-up Phase was completed. The 2 urine tests were added to obtain a more sensitive measure of renal function. Text modified to include urine samples for future testing. Blood and urine samples were collected and stored for future safety testing if necessary.
23 February 2010	CRP inclusion criterion was modified to reflect changes in the normal range at the central lab over a period of time. As the normal value is ≤ 5 mg/L this new CRP represents a value 140% above the upper limit of normal (ULN). Added history of tuberculosis in exclusion criteria 5 to ensure subjects with higher risk (ie, history of TB) were not enrolled. Subjects with very low lymphocyte counts at screening were to be excluded from the study. Additional information was added to the protocol to help investigators determine the severity of injection site reactions that may occur in the study. Overdose language was clarified to ensure that dosing errors do not occur.
02 December 2010	The timing of vital signs was changed to correspond to the change in amount of time that subjects are required to stay at the site after dosing on days 1, 15, and 84. Chest x-ray was to be performed within 24 weeks of the screening visit documenting the absence of any significant findings was available, the screening X-ray was not required. On-site post-dose safety monitoring period was reduced as subjects were required to stay at the site for at least 6 hours after dosing on days 1, 15 and 84.
12 November 2012	Two new subject discontinuation criteria were added: subjects with B-cell levels that achieved a new stable baseline or subjects who completed 2 years of follow-up after the last dose of study drug administration. The recommended list of repeated laboratory tests was updated to include prothrombin time. More inclusive definition of AEs and of SAEs were added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Certain secondary outcome measures (hybrid measure of ACR, ACR--N, ACR--n curve, EULAR response) were not analyzed due to the Sponsor's decision to terminate development of the compound.

Notes: