Clinical trial results:
A Phase IIB , Randomized, Multi-Center, Double-Blind, Dose-Ranging, Placebo/Active Controlled Study to Evaluate the Efficacy and Safety of BMS-945429 Subcutaneous Injection With or Without Methotrexate in Subjects with Moderate to Severe Rheumatoid Arthritis with Inadequate Response to Methotrexate

Summary

EudraCT number	2010-023956-99
Trial protocol	HU BE NL DE CZ ES IT
Global end of trial date	10 June 2015

Results information

Result version number	v1 (current)
This version publication date	20 February 2023
First version publication date	20 February 2023

Trial information

Trial identification

Sponsor protocol code	IM133-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01373151
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	CSL Behring
Sponsor organisation address	1020 First Avenue, King of Prussia, United States, 19406
Public contact	Study Director, CSL Behring, +1 610-878-4000, clinicaltrials@cslbehring.com
Scientific contact	Study Director, CSL Behring, +1 610-878-4000, clinicaltrials@cslbehring.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	10 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 June 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of BMS-945429 SC versus placebo (PBO) on a background of MTX as assessed by ACR20 response rates at 12 weeks.

Protection of trial subjects:

Standard of care procedures were employed in order to minimize harm to the patients. Study staff continuously interacted with the patients and were thoroughly trained on patient rights as well as medically trained to handle any adverse events. Study staff were well-informed on procedures to handle subjects from pre-screening through the completion of the study. All patients were explained the alternatives to being a part of the study. Procedures were also in place to ensure there was no undue coercion during the informed consent process.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 20
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Czech Republic: 10
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Argentina: 102
Country: Number of subjects enrolled	Brazil: 32
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Japan: 58
Country: Number of subjects enrolled	Korea, Republic of: 4
Country: Number of subjects enrolled	Mexico: 70
Country: Number of subjects enrolled	Russian Federation: 39
Country: Number of subjects enrolled	South Africa: 18
Country: Number of subjects enrolled	Taiwan: 7
Country: Number of subjects enrolled	United States: 10

Worldwide total number of subjects	418
EEA total number of subjects	76

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)	366
From 65 to 84 years	52
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 841 were enrolled and 418 were randomized and treated with study drug.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo+MTX

Arm description:

BMS-945429 (Clazakizumab)Placebo/BMS-945429+Methotrexate+Adalimumab Placebo

BMS-945429 Placebo: Injection, Subcutaneous, 0 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, Day 1 - Week 24 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

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

Dosage and administration details:

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm title	Clazakizumab(25)+MTX

Arm description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm type	Experimental
Investigational medicinal product name	Clazakizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

BMS-945429: Injection, Subcutaneous

Arm title	Clazakizumab(100)

Arm description:
BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm type	Experimental
Investigational medicinal product name	Clazakizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
BMS-945429: Injection, Subcutaneous

Arm title	Clazakizumab(100)+MTX

Arm description:
BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 25 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm type	Experimental
Investigational medicinal product name	Clazakizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
BMS-945429: Injection, Subcutaneous

Arm title	Clazakizumab(200)

Arm description:
BMS-945429 + Methotrexate/Methotrexate Placebo + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm type	Experimental
Investigational medicinal product name	Clazakizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
BMS-945429: Injection, Subcutaneous

Arm title	Clazakizumab(200)+MTX

Arm description:
BMS-945429 + Methotrexate/Methotrexate Placebo+Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm type	Experimental
Investigational medicinal product name	Clazakizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
BMS-945429: Injection, Subcutaneous

Arm title	ADA+MTX

Arm description:
Adalimumab(ADA) + Methotrexate

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab: Injection, Subcutaneous, 40 mg, Every 2 weeks, 48 weeks

Arm type	Active comparator
Investigational medicinal product name	ADALIMUMAB
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
Injection, Subcutaneous

Number of subjects in period 1	Placebo+MTX	Clazakizumab(25)+ MTX	Clazakizumab(100)
Started	61	59	60
Completed	56	59	56
Not completed	5	0	4
Consent withdrawn by subject	2	-	3
Adverse event, non-fatal	-	-	1
Lack of efficacy	3	-	-

Number of subjects in period 1	Clazakizumab(100)+ MTX	Clazakizumab(200)	Clazakizumab(200)+ MTX
Started	60	59	60
Completed	59	54	56
Not completed	1	5	4
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	-	4	3
Lack of efficacy	-	1	-

Number of subjects in period 1	ADA+MTX
Started	59
Completed	59
Not completed	0
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Lack of efficacy	-

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo+MTX

Arm description:

BMS-945429 (Clazakizumab)Placebo/BMS-945429+Methotrexate+Adalimumab Placebo

BMS-945429 Placebo: Injection, Subcutaneous, 0 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, Day 1 - Week 24 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

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

Dosage and administration details:

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm title	Clazakizumab(25)+MTX

Arm description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm type	Experimental

Investigational medicinal product name	Clazakizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
BMS-945429: Injection, Subcutaneous

Arm title	Clazakizumab(100)

Arm description:
BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm type	Experimental
Investigational medicinal product name	Clazakizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
BMS-945429: Injection, Subcutaneous

Arm title	Clazakizumab(100)+MTX

Arm description:
BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 25 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm type	Experimental
Investigational medicinal product name	Clazakizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
BMS-945429: Injection, Subcutaneous

Arm title	Clazakizumab(200)

Arm description:
BMS-945429 + Methotrexate/Methotrexate Placebo + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm type	Experimental

Investigational medicinal product name	Clazakizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
BMS-945429: Injection, Subcutaneous

Arm title	Clazakizumab(200)+MTX

Arm description:
BMS-945429 + Methotrexate/Methotrexate Placebo+Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Arm type	Experimental
Investigational medicinal product name	Clazakizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
BMS-945429: Injection, Subcutaneous

Arm title	ADA+MTX

Arm description:
Adalimumab(ADA) + Methotrexate

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab: Injection, Subcutaneous, 40 mg, Every 2 weeks, 48 weeks

Arm type	Active comparator
Investigational medicinal product name	ADALIMUMAB
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
Injection, Subcutaneous

Number of subjects in period 2[1]	Placebo+MTX	Clazakizumab(25)+ MTX	Clazakizumab(100)
Started	56	58	56
Completed	47	57	52
Not completed	9	1	4
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	3
Unknown	-	-	1

subject request to discontinue	-	1	-
Lack of efficacy	9	-	-

Number of subjects in period 2[1]	Clazakizumab(100)+ MTX	Clazakizumab(200)	Clazakizumab(200)+ MTX
Started	59	54	55
Completed	54	52	55
Not completed	5	2	0
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	3	-	-
Unknown	-	-	-
subject request to discontinue	-	-	-
Lack of efficacy	1	2	-

Number of subjects in period 2[1]	ADA+MTX
Started	59
Completed	54
Not completed	5
Consent withdrawn by subject	-
Adverse event, non-fatal	1
Unknown	1
subject request to discontinue	-
Lack of efficacy	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Only subjects treated in Period 2 were counted.

Baseline characteristics

Reporting groups

Reporting group title	Placebo+MTX

Reporting group description:

BMS-945429 (Clazakizumab)Placebo/BMS-945429+Methotrexate+Adalimumab Placebo

BMS-945429 Placebo: Injection, Subcutaneous, 0 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, Day 1 - Week 24 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(25)+MTX

Reporting group description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(100)

Reporting group description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(100)+MTX

Reporting group description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 25 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(200)

Reporting group description:

BMS-945429 + Methotrexate/Methotrexate Placebo + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(200)+MTX

Reporting group description:

BMS-945429 + Methotrexate/Methotrexate Placebo+Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	ADA+MTX

Reporting group description:

Adalimumab(ADA) + Methotrexate

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab: Injection, Subcutaneous, 40 mg, Every 2 weeks, 48 weeks

Reporting group values	Placebo+MTX	Clazakizumab(25)+ MTX	Clazakizumab(100)
Number of subjects	61	59	60
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	54	56	47
From 65-84 years	7	3	13
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	51.4	47.4	55.0
standard deviation	± 11.03	± 10.97	± 12.21
Gender categorical Units: Subjects			
Female	46	46	52
Male	15	13	8

Reporting group values	Clazakizumab(100)+ MTX	Clazakizumab(200)	Clazakizumab(200)+ MTX
Number of subjects	60	59	60
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	52	51	55
From 65-84 years	8	8	5
85 years and over	0	0	0

Age continuous			
Units: years			
arithmetic mean	49.9	50.0	46.4
standard deviation	± 13.95	± 12.53	± 11.91
Gender categorical			
Units: Subjects			
Female	53	49	49
Male	7	10	11

Reporting group values	ADA+MTX	Total	
Number of subjects	59	418	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	51	366	
From 65-84 years	8	52	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	52.8		
standard deviation	± 11.41	-	
Gender categorical			
Units: Subjects			
Female	48	343	
Male	11	75	

End points

End points reporting groups

Reporting group title	Placebo+MTX

Reporting group description:

BMS-945429 (Clazakizumab)Placebo/BMS-945429+Methotrexate+Adalimumab Placebo

BMS-945429 Placebo: Injection, Subcutaneous, 0 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, Day 1 - Week 24 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(25)+MTX

Reporting group description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(100)

Reporting group description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(100)+MTX

Reporting group description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 25 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(200)

Reporting group description:

BMS-945429 + Methotrexate/Methotrexate Placebo + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(200)+MTX

Reporting group description:

BMS-945429 + Methotrexate/Methotrexate Placebo+Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	ADA+MTX

Reporting group description:
Adalimumab(ADA) + Methotrexate

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab: Injection, Subcutaneous, 40 mg, Every 2 weeks, 48 weeks

Reporting group title	Placebo+MTX

Reporting group description:
BMS-945429 (Clazakizumab)Placebo/BMS-945429+Methotrexate+Adalimumab Placebo

BMS-945429 Placebo: Injection, Subcutaneous, 0 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, Day 1 - Week 24 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(25)+MTX

Reporting group description:
BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(100)

Reporting group description:
BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(100)+MTX

Reporting group description:
BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 25 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(200)

Reporting group description:
BMS-945429 + Methotrexate/Methotrexate Placebo + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(200)+MTX

Reporting group description:

BMS-945429 + Methotrexate/Methotrexate Placebo+Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	ADA+MTX

Reporting group description:

Adalimumab(ADA) + Methotrexate

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab: Injection, Subcutaneous, 40 mg, Every 2 weeks, 48 weeks

Primary: Percent of Participants Achieving an American College of Rheumatology (ACR) 20% Response Rate

End point title	Percent of Participants Achieving an American College of Rheumatology (ACR) 20% Response Rate[1]

End point description:

The ACR20/50/70 is a composite measure defined as both improvement of 20%, 50% or 70% in the number of tender and number of swollen joints, and a 20%, 50% or 70% improvement in three of the following five criteria: patient global assessment, physician global assessment, functional ability measure [most often Health Assessment Questionnaire (HAQ)], visual analog pain scale, and erythrocyte sedimentation rate or C-reactive protein (CRP).

End point type	Primary

End point timeframe:

At 12 Weeks

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: Descriptive statistics were used.

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	60	60
Units: percentage of participants				
number (not applicable)	39.3	76.3	55.0	73.3

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: percentage of participants				
number (not applicable)	61.0	60.0	76.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants With ACR 20 Response

End point title	Percent of Participants With ACR 20 Response

End point description:

The ACR20/50/70 is a composite measure defined as both improvement of 20%, 50% or 70% in the number of tender and number of swollen joints, and a 20%, 50% or 70% improvement in three of the following five criteria: patient global assessment, physician global assessment, functional ability measure [most often Health Assessment Questionnaire (HAQ)], visual analog pain scale, and erythrocyte sedimentation rate or C-reactive protein (CRP).

End point type	Secondary

End point timeframe:

At 24 weeks

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	60	60
Units: percentage of participants				
number (not applicable)	37.7	81.4	58.3	65.0

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: percentage of participants				
number (not applicable)	57.6	66.7	66.1	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants Achieving ACR 50 Response Rate

End point title	Percent of Participants Achieving ACR 50 Response Rate

End point description:

The ACR20/50/70 is a composite measure defined as both improvement of 20%, 50% or 70% in the number of tender and number of swollen joints, and a 20%, 50% or 70% improvement in three of the following five criteria: patient global assessment, physician global assessment, functional ability measure [most often Health Assessment Questionnaire (HAQ)], visual analog pain scale, and erythrocyte sedimentation rate or C-reactive protein (CRP).

End point type	Secondary

End point timeframe:

At weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	60	60
Units: percentage of participants				
number (not applicable)				
12 weeks	21.3	49.2	26.7	43.3
24 weeks	16.4	47.5	36.7	46.7

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: percentage of participants				
number (not applicable)				
12 weeks	28.8	26.7	30.5	
24 weeks	33.9	43.3	47.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants Achieving ACR 70 Response Rate

End point title	Percent of Participants Achieving ACR 70 Response Rate

End point description:

The ACR20/50/70 is a composite measure defined as both improvement of 20%, 50% or 70% in the number of tender and number of swollen joints, and a 20%, 50% or 70% improvement in three of the following five criteria: patient global assessment, physician global assessment, functional ability measure [most often Health Assessment Questionnaire (HAQ)], visual analog pain scale, and erythrocyte sedimentation rate or C-reactive protein (CRP).

End point type	Secondary

End point timeframe:

At weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	60	60
Units: percentage of participants				
number (not applicable)				
12 weeks	8.2	18.6	13.3	26.7
24 weeks	6.6	27.1	16.7	40.0

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: percentage of participants				
number (not applicable)				
12 weeks	11.9	13.3	11.9	
24 weeks	25.4	30.0	18.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Disease Activity as Measured by Disease Activity Score 28 C-reactive Protein (DAS28-CRP)

End point title	Mean Change From Baseline in Disease Activity as Measured by Disease Activity Score 28 C-reactive Protein (DAS28-CRP)

End point description:

DAS28-CRP = Disease Activity Scores 28 based on C Reactive Protein. A DAS28-CRP below 2.6 is interpreted as remission.

End point type	Secondary

End point timeframe:

Baseline, weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61[2]	59[3]	60[4]	60[5]
Units: score on a scale				
arithmetic mean (standard error)				
12 weeks	-1.15 (± 0.1652)	-2.65 (± 0.1610)	-2.29 (± 0.1603)	-2.68 (± 0.1597)
24 weeks	-1.69 (± 0.1825)	-3.01 (± 0.1684)	-2.60 (± 0.1719)	-3.06 (± 0.1713)

Notes:

[2] - n=52 for week 12; n=43 for week 24

[3] - n=54 for week 12; n=56 for week 24

[4] - n=55 for week 12; n=50 for week 24

[5] - n=56 for week 12; n=51 for week 24

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59[6]	60[7]	59[8]	
Units: score on a scale				

arithmetic mean (standard error)				
12 weeks	-2.34 (± 0.1665)	-2.52 (± 0.1610)	-2.04 (± 0.1647)	
24 weeks	-2.55 (± 0.1769)	-2.95 (± 0.1706)	-2.52 (± 0.1769)	

Notes:

[6] - n=50 for week 12; n=47 for week 24

[7] - n=54 for week 12; n=53 for week 24

[8] - n=54 for week 12; n=49 for week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants With Remission by DAS28-CRP

End point title	Percent of Participants With Remission by DAS28-CRP

End point description:

DAS28-CRP = Disease Activity Scores 28 based on C Reactive Protein. A DAS28-CRP below 2.6 is interpreted as remission.

End point type	Secondary

End point timeframe:

At weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	60	60
Units: percentage of participants				
number (not applicable)				
week 12	1.6	35.6	21.7	35.0
week 24	11.5	49.2	25.0	40.0

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: percentage of participants				
number (not applicable)				
week 12	25.4	26.7	20.3	
week 24	35.6	41.7	23.7	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Clinical Disease Activity Index (CDAI)

End point title	Mean Change From Baseline in Clinical Disease Activity Index (CDAI)

End point description:

CDAI is a composite index for assessing disease activity. CDAI is based on the simple summation of the count of swollen joint count (SCJ) (0-28) and tender joint count (TJC) (0-28) along with patient global assessment (0-10) Scale and physician global assessment (0-10) for estimating disease activity where 10 means maximal activity. The CDAI has a range from 0 to 76.

CDAI <= 2.8 = Remission; CDAI > 2.8 and <= 10 = Low Disease Activity; CDAI > 10 and <= 22 = Moderate Disease Activity; CDAI > 22 = High Disease Activity

End point type	Secondary

End point timeframe:

Baseline, weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61[9]	59[10]	60[11]	60[12]
Units: score on a scale				
arithmetic mean (standard error)				
week 12	-14.5 (± 1.727)	-22.7 (± 1.686)	-17.7 (± 1.687)	-23.1 (± 1.701)
week 24	-20.3 (± 1.703)	-26.1 (± 1.587)	-22.0 (± 1.613)	-26.9 (± 1.622)

Notes:

[9] - n=54 for week 12; n=45 for week 24

[10] - n=58 for week 12; n=57 for week 24

[11] - n=55 for week 12; n=51 for week 24

[12] - n=56 for week 12; n=52 for week 24

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59[13]	60[14]	59[15]	
Units: score on a scale				
arithmetic mean (standard error)				
week 12	-19.8 (± 1.738)	-21.0 (± 1.697)	-22.4 (± 1.702)	
week 24	-21.7 (± 1.643)	-25.6 (± 1.606)	-26.2 (± 1.631)	

Notes:

[13] - n=52 for week 12; n=50 for week 24

[14] - n=55 for week 12; n=54 for week 24

[15] - n=57 for week 12; n=52 for week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants With Remission by CDAI

End point title	Percent of Participants With Remission by CDAI

End point description:

CDAI is a composite index for assessing disease activity. CDAI is based on the simple summation of the count of swollen joint count (SCJ) (0-28) and tender joint count (TJC) (0-28) along with patient global assessment (0-10) Scale and physician global assessment (0-10) for estimating disease activity where 10 means maximal activity. The CDAI has a range from 0 to 76.

CDAI <= 2.8 = Remission; CDAI > 2.8 and <= 10 = Low Disease Activity; CDAI > 10 and <= 22 = Moderate Disease Activity; CDAI > 22 = High Disease Activity

End point type	Secondary

End point timeframe:

At weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	60	60
Units: percentage of participants				
number (not applicable)				
week 12	3.3	11.9	8.3	8.3
week 24	1.6	15.3	6.7	21.7

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: percentage of participants				
number (not applicable)				
week 12	3.4	3.3	8.5	
week 24	6.8	20.0	8.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Simplified Disease Activity Index (SDAI)

End point title	Mean Change From Baseline in Simplified Disease Activity Index (SDAI)

End point description:

SDAI is a composite index for assessing disease activity. SDAI is based on the simple summation of the count of swollen joint count (0-28) and tender joint count (0-28) along with patient global assessment (0-10) Scale and physician global assessment (0-10) for estimating disease activity where 10 means maximal activity and C-reactive protein (0-10). The SDAI has a range from 0 to 86.

0.0 - 3.3 = Remission; 3.4 - 11.0 = Low Activity; 11.1 - 26.0 = Moderate Activity; 26.1 - 86.0 = High Activity

End point type	Secondary

End point timeframe:

Baseline, weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61[16]	59[17]	60[18]	60[19]
Units: score on a scale				
arithmetic mean (standard error)				
week 12	-14.5 (± 1.794)	-24.9 (± 1.749)	-20.4 (± 1.745)	-25.3 (± 1.734)
week 24	-20.6 (± 1.812)	-28.4 (± 1.670)	-24.5 (± 1.704)	-29.1 (± 1.698)

Notes:

[16] - n=52 for week 12; n=43 for week 24

[17] - n=54 for week 12; n=56 for week 24

[18] - n=54 for week 12; n=50 for week 24

[19] - n=56 for week 12; n=51 for week 24

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59[20]	60[21]	59[22]	
Units: score on a scale				
arithmetic mean (standard error)				
week 12	-22.2 (± 1.811)	-23.3 (± 1.747)	-23.2 (± 1.785)	
week 24	-23.5 (± 1.755)	-27.6 (± 1.691)	-27.6 (± 1.752)	

Notes:

[20] - n=50 for week 12; n=47 for week 24

[21] - n=54 for week 12; n=53 for week 24

[22] - n=54 for week 12; n=49 for week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants With Remission by SDAI

End point title	Percent of Participants With Remission by SDAI

End point description:

SDAI is a composite index for assessing disease activity. SDAI is based on the simple summation of the count of swollen joint count (0-28) and tender joint count (0-28) along with patient global assessment (0-10) Scale and physician global assessment (0-10) for estimating disease activity where 10 means maximal activity and C-reactive protein (0-10). The SDAI has a range from 0 to 86.

0.0 - 3.3 = Remission; 3.4 - 11.0 = Low Activity; 11.1 - 26.0 = Moderate Activity; 26.1 - 86.0 = High Activity

End point type	Secondary

End point timeframe:

At weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	60	60
Units: percentage of participants				
number (not applicable)				
week 12	1.6	11.9	8.3	8.3
week 24	4.9	18.6	6.7	20.0

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: percentage of participants				
number (not applicable)				
week 12	6.8	5.0	10.2	
week 24	6.8	23.3	8.5	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants With Remission Rate by Boolean Definition

End point title	Percent of Participants With Remission Rate by Boolean Definition

End point description:

Boolean-based definition:

At any time point, a patient must satisfy all of the following:

TJC ≤1 (0-28); SJC ≤1 (0-28); CRP ≤1 mg/dl; Patient Global Assessment ≤1 (on a 0-10 scale)

End point type	Secondary

End point timeframe:

At weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	60	60
Units: percentage of participants				
number (not applicable)				
week 12	3.3	8.5	6.7	10.0
week 24	1.6	10.2	5.0	13.3

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: percentage of participants				
number (not applicable)				
week 12	1.7	5.0	5.1	
week 24	5.1	18.3	10.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Health Assessment Questionnaire (HAQ) Disability Index

End point title	Mean Change From Baseline in Health Assessment Questionnaire (HAQ) Disability Index

End point description:

Patients report the amount of difficulty they have in performing 8 categories. Each category is scored on a scale ranging from 0 (performed without any difficulty) to 3 (cannot be done at all). The HAQ-DI is then calculated by summing the scores and dividing by the number of categories answered. Total score is between 0-3.0. Increasing scores indicate worse functioning with 0 indicating no functional impairment and 3 indicating complete impairment. The HAQ-DI cannot be calculated if the subject does not have scores for at least 6 categories. A response was defined as a subject with a reduction from baseline in HAQ-DI of at least 0.22.

End point type	Secondary

End point timeframe:

Baseline, weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61[23]	59[24]	60[25]	60[26]
Units: score on a scale				
arithmetic mean (standard error)				
week 12	-0.44 (± 0.0827)	-0.66 (± 0.0801)	-0.47 (± 0.0807)	-0.70 (± 0.0811)
week 24	-0.62 (± 0.0861)	-0.68 (± 0.0806)	-0.64 (± 0.0823)	-0.79 (± 0.0823)

Notes:

[23] - n=54 for week 12; n=44 for week 24

[24] - n=59 for week 12; n=58 for week 24

[25] - n=56 for week 12; n=51 for week 24

[26] - n=57 for week 12; n=53 for week 24

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59[27]	60[28]	59[29]	
Units: score on a scale				

arithmetic mean (standard error)				
week 12	-0.51 (± 0.0834)	-0.60 (± 0.0807)	-0.60 (± 0.0819)	
week 24	-0.60 (± 0.0840)	-0.71 (± 0.0811)	-0.66 (± 0.0833)	

Notes:

[27] - n=52 for week 12; n=50 for week 24

[28] - n=56 for week 12; n=56 for week 24

[29] - n=58 for week 12; n=53 for week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Short Form 36 (SF-36) as Measured by Physical and Mental Components

End point title	Mean Change From Baseline in Short Form 36 (SF-36) as Measured by Physical and Mental Components

End point description:

The SF-36 questionnaire consists of eight scales yielding two summary measures: physical and mental health. The physical health measure includes four scales of physical functioning (10 items), role-physical (4 items), bodily pain (2 items), and general health (5 items). The mental health measure is composed of vitality (4 items), social functioning (2 items), role-emotional (3 items), and mental health (5 items). To score the SF-36, scales are standardized with a scoring algorithm to obtain a score ranging from 0 to 100. Higher scores indicate better health status.

End point type	Secondary

End point timeframe:

Baseline, weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61[30]	59[31]	60[32]	60[33]
Units: score on a scale				
arithmetic mean (standard error)				
Mental component (week 12)	5.3 (± 1.274)	5.9 (± 1.240)	4.5 (± 1.251)	7.3 (± 1.244)
Mental component (week 24)	6.0 (± 1.327)	6.4 (± 1.208)	6.6 (± 1.247)	7.5 (± 1.247)
Physical component (week 12)	4.0 (± 1.030)	7.5 (± 0.999)	7.3 (± 1.010)	9.5 (± 1.002)
Physical component (week 24)	6.2 (± 1.149)	8.6 (± 1.045)	9.4 (± 1.080)	10.9 (± 1.076)

Notes:

[30] - n=55 for week 12; n=46 for week 24

[31] - n=58 for week 12; n=59 for week 24

[32] - n=57 for week 12; n=54 for week 24

[33] - n=58 for week 12; n=54 for week 24

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59[34]	60[35]	59[36]	
Units: score on a scale				
arithmetic mean (standard error)				
Mental component (week 12)	4.0 (± 1.283)	5.7 (± 1.230)	6.4 (± 1.250)	

Mental component (week 24)	5.3 (± 1.271)	8.0 (± 1.219)	7.1 (± 1.246)	
Physical component (week 12)	6.8 (± 1.028)	7.3 (± 0.994)	8.4 (± 1.006)	
Physical component (week 24)	7.7 (± 1.094)	8.2 (± 1.057)	8.2 (± 1.077)	

Notes:

[34] - n=55 for week 12; n=53 for week 24

[35] - n=59 for week 12; n=57 for week 24

[36] - n=58 for week 12; n=55 for week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Fatigue Severity (VAS) Score

End point title	Mean Change From Baseline in Fatigue Severity (VAS) Score

End point description:

A 9-item questionnaire with questions related to how fatigue interferes with certain activities and rates its severity according to a self-report scale. The items are scored on a 7 point scale with 1 = strongly disagree and 7= strongly agree. The minimum score = 9 and maximum score possible = 63. Higher the score = greater fatigue severity.

End point type	Secondary

End point timeframe:

Baseline, weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61[37]	59[38]	60[39]	60[40]
Units: score on a scale				
arithmetic mean (standard error)				
week 12	-14.3 (± 3.146)	-20.8 (± 3.060)	-19.4 (± 3.077)	-27.4 (± 3.077)
week 24	-12.9 (± 3.306)	-23.9 (± 3.052)	-22.3 (± 3.131)	-31.3 (± 3.103)

Notes:

[37] - n=54 for week 12; n=45 for week 24

[38] - n=58 for week 12; n=57 for week 24

[39] - n=56 for week 12; n=51 for week 24

[40] - n=57 for week 12; n=54 for week 24

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59[41]	60[42]	59[43]	
Units: score on a scale				
arithmetic mean (standard error)				
week 12	-21.7 (± 3.180)	-18.6 (± 3.056)	-26.3 (± 3.080)	
week 24	-17.7 (± 3.184)	-23.4 (± 3.056)	-27.0 (± 3.134)	

Notes:

[41] - n=52 for week 12; n=50 for week 24

[42] - n=57 for week 12; n=56 for week 24

[43] - n=58 for week 12; n=53 for week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) Scores

End point title	Mean Change From Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) Scores

End point description:

The WPAI yeilds four types of scores:
1.Absenteeism (work time missed)
2.Presenteesism (impairment at work / reduced on-the-job effectiveness)
3.Work productivty loss (overall work impairment / absenteeism plus presenteeism)
4.Activity Impairment WPAI outcomes are expressed as impairment percentages with each subscale score ranging from 0-100. The subscale scores are added and averaged to produce a total WPAI score between 0-100. Higher scores indicate greater impairment and less productivity.

End point type	Secondary

End point timeframe:

Baseline, weeks 12 and 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61[44]	59[45]	60[46]	60[47]
Units: score on a scale				
arithmetic mean (standard error)				
week 12	-9.6 (± 3.273)	-2.2 (± 3.443)	-8.7 (± 3.673)	-12.0 (± 3.081)
week 24	-10.7 (± 4.033)	-1.8 (± 3.893)	-17.1 (± 4.200)	-12.1 (± 3.448)

Notes:

[44] - n=22 for week 12; n=18 for week 24

[45] - n=20 for week 12; n=20 for week 24

[46] - n=18 for week 12; n=17 for week 24

[47] - n=25 for week 12; n=25 for week 24

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59[48]	60[49]	59[50]	
Units: score on a scale				
arithmetic mean (standard error)				
week 12	-13.7 (± 3.285)	-10.0 (± 3.575)	-11.7 (± 6.281)	
week 24	-5.9 (± 3.788)	-12.6 (± 3.938)	-4.7 (± 6.379)	

Notes:

[48] - n=22 for week 12; n=21 for week 24

[49] - n=19 for week 12; n=19 for week 24

[50] - n=6 for week 12; n=7 for week 24

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Radiographic (MRI) Progression of Synovitis, Osteitis (Bone Marrow Edema), Bone Erosion and Cartilage Loss (Joint-space Narrowing)

End point title	Mean Change From Baseline in Radiographic (MRI) Progression of Synovitis, Osteitis (Bone Marrow Edema), Bone Erosion and Cartilage Loss (Joint-space Narrowing)

End point description:

End point type	Secondary

End point timeframe:

Baseline and week 12

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61[51]	59[52]	60[53]	60[54]
Units: cubic millimeters				
arithmetic mean (standard error)				
Erosion	1.3 (± 0.352)	0.4 (± 0.341)	1.1 (± 0.356)	0.3 (± 0.334)
Edema	0.2 (± 1.009)	-6.4 (± 0.993)	-2.6 (± 1.015)	-4.7 (± 0.998)
Synovitis	-0.5 (± 0.436)	-2.5 (± 0.427)	-1.4 (± 0.440)	-2.2 (± 0.426)
Narrowing	0.1 (± 0.133)	-0.1 (± 0.130)	0.2 (± 0.135)	-0.1 (± 0.126)

Notes:

[51] - n=51

[52] - n=50 for erosion and narrowing; n=51 for edema and syovitis

[53] - n=50

[54] - n=59

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59[55]	60[56]	59[57]	
Units: cubic millimeters				
arithmetic mean (standard error)				
Erosion	1.0 (± 0.369)	-0.2 (± 0.341)	-0.5 (± 0.348)	
Edema	-4.6 (± 1.036)	-5.1 (± 0.993)	-3.1 (± 1.008)	
Synovitis	-2.9 (± 0.447)	-2.5 (± 0.427)	-2.9 (± 0.435)	
Narrowing	0.1 (± 0.139)	0.0 (± 0.129)	-0.2 (± 0.132)	

Notes:

[55] - n=48 for erosion and narrowing; n=50 for edema and synovitis

[56] - n=54

[57] - n=52

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Radiographic (X-ray) Progression of Joint Damage as Measured by Modified Sharp/Van Der Heijde Total Score

End point title	Mean Change From Baseline in Radiographic (X-ray) Progression of Joint Damage as Measured by Modified Sharp/Van Der Heijde Total Score

End point description:

The Sharp-van der Heijde total score ranges from 0-528. Scores for erosion range from 0 to 5 in the hands and 0 to 10 in the feet and reflect erosion size, with 0 defined as no erosion and 3 defined as a large erosion passing the midline of the joint. If there is >1 erosion per joint, scores can be combined to give a maximum score of 5 per joint in the hands and 10 per joint in the feet (a maximum of 5 at each side of the joint). Joint space narrowing scores vary from 0 to 4 in both the hands and feet, with 0 being normal and 4 being the absence of joint space with evident ankylosis or subluxation. Gross osteolysis and pencil-in-cup change are scored separately and, if present, are assigned the maximum score for erosion and joint space narrowing for the same affected joint. Higher scores indicate increased joint damage.

End point type	Secondary

End point timeframe:

Baseline and week 24

End point values	Placebo+MTX	Clazakizumab(25)+MTX	Clazakizumab(100)	Clazakizumab(100)+MTX
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	59	54	54
Units: score on a scale				
arithmetic mean (standard error)	1.8 (± 0.353)	0.3 (± 0.320)	0.0 (± 0.327)	0.1 (± 0.324)

End point values	Clazakizumab(200)	Clazakizumab(200)+MTX	ADA+MTX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	53	54	
Units: score on a scale				
arithmetic mean (standard error)	0.1 (± 0.330)	0.1 (± 0.336)	0.1 (± 0.333)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 48 weeks per participant

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Placebo+MTX

Reporting group description:

BMS-945429 (Clazakizumab)Placebo/BMS-945429+Methotrexate+Adalimumab Placebo

BMS-945429 Placebo: Injection, Subcutaneous, 0 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, Day 1 - Week 24 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(25)+MTX

Reporting group description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(100)

Reporting group description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(100)+MTX

Reporting group description:

BMS-945429 + Methotrexate + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 25 mg, Every 4 weeks, Day 1 - Week 24 only

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, Week 25 - Week 48

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(200)

Reporting group description:

BMS-945429 + Methotrexate/Methotrexate Placebo + Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 200 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	Clazakizumab(200)+MTX

Reporting group description:

BMS-945429 + Methotrexate/Methotrexate Placebo+Adalimumab Placebo

BMS-945429: Injection, Subcutaneous, 100 mg, Every 4 weeks, 48 weeks

Methotrexate Placebo: Tablets, Oral, 0 mg, Weekly, Day 1 - Week 24 only

Methotrexate: Tablets, Oral, 15 mg, Weekly, Week 25 - Week 48 only

Adalimumab Placebo: Injection, Subcutaneous, 0 mg, Every 2 weeks, 48 weeks

Reporting group title	ADA+MTX

Reporting group description:

Adalimumab(ADA) + Methotrexate

Methotrexate: Tablets, Oral, 15 mg, Weekly, 48 weeks

Adalimumab: Injection, Subcutaneous, 40 mg, Every 2 weeks, 48 weeks

Serious adverse events	Placebo+MTX	Clazakizumab(25)+ MTX	Clazakizumab(100)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 61 (3.28%)	5 / 59 (8.47%)	5 / 60 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Lung disorder			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Suicide attempt			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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			
Foot fracture			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 60 (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
Humerus fracture			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medication error			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Overdose			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 60 (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			
Acute coronary syndrome			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 60 (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
Atrial fibrillation			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Coronary artery disease			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Mitral valve incompetence			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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			
Headache			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 60 (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
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
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			
Cataract			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal wall haematoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Diarrhoea			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	0 / 60 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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			
Appendicitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Cellulitis			
subjects affected / exposed	0 / 61 (0.00%)	2 / 59 (3.39%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Pulmonary tuberculosis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Atypical pneumonia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Bursitis infective			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Herpes zoster			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Infective tenosynovitis			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Pneumocystis jiroveci pneumonia			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Sepsis			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Traumatic haematoma			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Clazakizumab(100)+ MTX	Clazakizumab(200)	Clazakizumab(200)+ MTX
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 60 (8.33%)	8 / 59 (13.56%)	5 / 60 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Hypertension			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	0 / 60 (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
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			

subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Suicide attempt			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	0 / 60 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	0 / 60 (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
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	0 / 60 (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
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Humerus fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Medication error			

subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	0 / 60 (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
Overdose			
subjects affected / exposed	0 / 60 (0.00%)	3 / 59 (5.08%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Atrial fibrillation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	0 / 60 (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
Mitral valve incompetence			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	0 / 60 (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
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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

Eye disorders			
Cataract			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Gastrointestinal disorders			
Abdominal wall haematoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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			
Cholelithiasis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	0 / 60 (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
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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			
Appendicitis			
subjects affected / exposed	2 / 60 (3.33%)	0 / 59 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Pneumonia			

subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	0 / 60 (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
Pulmonary tuberculosis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 59 (1.69%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	0 / 60 (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
Herpes zoster			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Infective tenosynovitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Influenza			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jiroveci pneumonia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic haematoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (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
Urinary tract infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	0 / 60 (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

Serious adverse events	ADA+MTX		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 59 (5.08%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung disorder			

subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Medication error			

subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mitral valve incompetence			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Eye disorders			
Cataract			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal wall haematoma			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bursitis infective				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 59 (1.69%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infective tenosynovitis				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jiroveci pneumonia				
subjects affected / exposed	0 / 59 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Traumatic haematoma			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo+MTX	Clazakizumab(25)+ MTX	Clazakizumab(100)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 61 (39.34%)	43 / 59 (72.88%)	43 / 60 (71.67%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 61 (3.28%)	11 / 59 (18.64%)	2 / 60 (3.33%)
occurrences (all)	2	11	2
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 61 (0.00%)	8 / 59 (13.56%)	0 / 60 (0.00%)
occurrences (all)	0	8	0
Gamma-glutamyl transferease increased			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	2 / 60 (3.33%)
occurrences (all)	1	0	2
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	3 / 60 (5.00%)
occurrences (all)	0	0	3
Overdose			

subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 61 (8.20%)	2 / 59 (3.39%)	0 / 60 (0.00%)
occurrences (all)	5	2	0
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 61 (0.00%)	8 / 59 (13.56%)	9 / 60 (15.00%)
occurrences (all)	0	8	9
Ejection site erythema			
subjects affected / exposed	0 / 61 (0.00%)	2 / 59 (3.39%)	8 / 60 (13.33%)
occurrences (all)	0	2	8
Injection site rash			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	8 / 60 (13.33%)
occurrences (all)	0	1	8
Injection site dermatitis			
subjects affected / exposed	0 / 61 (0.00%)	4 / 59 (6.78%)	3 / 60 (5.00%)
occurrences (all)	0	4	3
Asthenia			
subjects affected / exposed	2 / 61 (3.28%)	1 / 59 (1.69%)	0 / 60 (0.00%)
occurrences (all)	2	1	0
Injection site hypersensitivity			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	3 / 60 (5.00%)
occurrences (all)	0	0	3
Injection site papule			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	2 / 60 (3.33%)
occurrences (all)	0	1	2
Injection site pruritis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
Injection site macule			

subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 61 (0.00%)	2 / 59 (3.39%)	4 / 60 (6.67%)
occurrences (all)	0	2	4
Leukopenia			
subjects affected / exposed	1 / 61 (1.64%)	0 / 59 (0.00%)	3 / 60 (5.00%)
occurrences (all)	1	0	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 61 (1.64%)	3 / 59 (5.08%)	1 / 60 (1.67%)
occurrences (all)	1	3	1
Nausea			
subjects affected / exposed	1 / 61 (1.64%)	3 / 59 (5.08%)	0 / 60 (0.00%)
occurrences (all)	1	3	0
Dyspepsia			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	0 / 60 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	3 / 60 (5.00%)
occurrences (all)	0	0	3
Skin lesion			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 61 (0.00%)	0 / 59 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	4 / 61 (6.56%)	2 / 59 (3.39%)	3 / 60 (5.00%)
occurrences (all)	4	2	3
Upper respiratory tract infection			
subjects affected / exposed	7 / 61 (11.48%)	5 / 59 (8.47%)	1 / 60 (1.67%)
occurrences (all)	7	5	1
Pharyngitis			
subjects affected / exposed	5 / 61 (8.20%)	2 / 59 (3.39%)	3 / 60 (5.00%)
occurrences (all)	5	2	3
Urinary tract infection			
subjects affected / exposed	4 / 61 (6.56%)	5 / 59 (8.47%)	1 / 60 (1.67%)
occurrences (all)	4	5	1
Bronchitis			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	2 / 60 (3.33%)
occurrences (all)	0	1	2
Herpes zoster			
subjects affected / exposed	0 / 61 (0.00%)	1 / 59 (1.69%)	1 / 60 (1.67%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	2 / 61 (3.28%)	7 / 59 (11.86%)	7 / 60 (11.67%)
occurrences (all)	2	7	7
Dyslipidaemia			
subjects affected / exposed	1 / 61 (1.64%)	7 / 59 (11.86%)	4 / 60 (6.67%)
occurrences (all)	1	7	4
Hypertriglyceridaemia			
subjects affected / exposed	2 / 61 (3.28%)	1 / 59 (1.69%)	1 / 60 (1.67%)
occurrences (all)	2	1	1
Hyperlipidaemia			
subjects affected / exposed	0 / 61 (0.00%)	3 / 59 (5.08%)	0 / 60 (0.00%)
occurrences (all)	0	3	0

Non-serious adverse events	Clazakizumab(100)+ MTX	Clazakizumab(200)	Clazakizumab(200)+ MTX
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 60 (85.00%)	43 / 59 (72.88%)	50 / 60 (83.33%)
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	13 / 60 (21.67%)	1 / 59 (1.69%)	1 / 60 (1.67%)
occurrences (all)	13	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	14 / 60 (23.33%)	0 / 59 (0.00%)	12 / 60 (20.00%)
occurrences (all)	14	0	12
Gamma-glutamyl transferease increased			
subjects affected / exposed	4 / 60 (6.67%)	0 / 59 (0.00%)	2 / 60 (3.33%)
occurrences (all)	4	0	2
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Overdose			
subjects affected / exposed	0 / 60 (0.00%)	3 / 59 (5.08%)	0 / 60 (0.00%)
occurrences (all)	0	3	0
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 60 (6.67%)	6 / 59 (10.17%)	2 / 60 (3.33%)
occurrences (all)	4	6	2
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	2 / 60 (3.33%)
occurrences (all)	0	1	2
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	11 / 60 (18.33%)	14 / 59 (23.73%)	9 / 60 (15.00%)
occurrences (all)	11	14	9
Ejection site erythema			
subjects affected / exposed	15 / 60 (25.00%)	10 / 59 (16.95%)	9 / 60 (15.00%)
occurrences (all)	15	10	9
Injection site rash			
subjects affected / exposed	8 / 60 (13.33%)	2 / 59 (3.39%)	8 / 60 (13.33%)
occurrences (all)	8	2	8
Injection site dermatitis			

subjects affected / exposed	4 / 60 (6.67%)	4 / 59 (6.78%)	7 / 60 (11.67%)
occurrences (all)	4	4	7
Asthenia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	3 / 60 (5.00%)
occurrences (all)	0	1	3
Injection site hypersensitivity			
subjects affected / exposed	2 / 60 (3.33%)	2 / 59 (3.39%)	1 / 60 (1.67%)
occurrences (all)	2	2	1
Injection site papule			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	3 / 60 (5.00%)
occurrences (all)	0	1	3
Injection site pruritis			
subjects affected / exposed	4 / 60 (6.67%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences (all)	4	0	1
Injection site macule			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	3 / 60 (5.00%)
occurrences (all)	0	1	3
Injection site pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 60 (3.33%)	4 / 59 (6.78%)	1 / 60 (1.67%)
occurrences (all)	2	4	1
Leukopenia			
subjects affected / exposed	2 / 60 (3.33%)	4 / 59 (6.78%)	3 / 60 (5.00%)
occurrences (all)	2	4	3
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 60 (5.00%)	2 / 59 (3.39%)	3 / 60 (5.00%)
occurrences (all)	3	2	3
Nausea			
subjects affected / exposed	0 / 60 (0.00%)	1 / 59 (1.69%)	2 / 60 (3.33%)
occurrences (all)	0	1	2
Dyspepsia			

subjects affected / exposed	1 / 60 (1.67%)	1 / 59 (1.69%)	0 / 60 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	0 / 60 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	3 / 60 (5.00%)
occurrences (all)	0	0	3
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	1 / 60 (1.67%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences (all)	1	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 60 (6.67%)	3 / 59 (5.08%)	7 / 60 (11.67%)
occurrences (all)	4	3	7
Upper respiratory tract infection			
subjects affected / exposed	3 / 60 (5.00%)	7 / 59 (11.86%)	1 / 60 (1.67%)
occurrences (all)	3	7	1
Pharyngitis			
subjects affected / exposed	3 / 60 (5.00%)	3 / 59 (5.08%)	3 / 60 (5.00%)
occurrences (all)	3	3	3
Urinary tract infection			
subjects affected / exposed	2 / 60 (3.33%)	2 / 59 (3.39%)	5 / 60 (8.33%)
occurrences (all)	2	2	5
Bronchitis			
subjects affected / exposed	0 / 60 (0.00%)	2 / 59 (3.39%)	2 / 60 (3.33%)
occurrences (all)	0	2	2
Herpes zoster			
subjects affected / exposed	1 / 60 (1.67%)	3 / 59 (5.08%)	0 / 60 (0.00%)
occurrences (all)	1	3	0
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	5 / 60 (8.33%)	5 / 59 (8.47%)	9 / 60 (15.00%)
occurrences (all)	5	5	9

Dyslipidaemia			
subjects affected / exposed	2 / 60 (3.33%)	2 / 59 (3.39%)	4 / 60 (6.67%)
occurrences (all)	2	2	4
Hypertriglyceridaemia			
subjects affected / exposed	2 / 60 (3.33%)	1 / 59 (1.69%)	1 / 60 (1.67%)
occurrences (all)	2	1	1
Hyperlipidaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 59 (0.00%)	1 / 60 (1.67%)
occurrences (all)	0	0	1

Non-serious adverse events	ADA+MTX		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 59 (59.32%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Gamma-glutamyl transferease increased			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Overdose			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Ejection site erythema			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Injection site rash			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Injection site dermatitis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Injection site hypersensitivity			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Injection site papule			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Injection site pruritis			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Injection site macule			
subjects affected / exposed	0 / 59 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Blood and lymphatic system disorders			

Neutropenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all)	2 / 59 (3.39%) 2 0 / 59 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all)	 6 / 59 (10.17%) 6 3 / 59 (5.08%) 3 3 / 59 (5.08%) 3		
Skin and subcutaneous tissue disorders Dermatitis allergic subjects affected / exposed occurrences (all) Skin lesion subjects affected / exposed occurrences (all)	 0 / 59 (0.00%) 0 0 / 59 (0.00%) 0		
Musculoskeletal and connective tissue disorders Muscle spasms subjects affected / exposed occurrences (all)	 4 / 59 (6.78%) 4		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Pharyngitis	 2 / 59 (3.39%) 2 0 / 59 (0.00%) 0 		

subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Herpes zoster			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		
Dyslipidaemia			
subjects affected / exposed	1 / 59 (1.69%)		
occurrences (all)	1		
Hypertriglyceridaemia			
subjects affected / exposed	3 / 59 (5.08%)		
occurrences (all)	3		
Hyperlipidaemia			
subjects affected / exposed	2 / 59 (3.39%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 January 2011	To permit the collection and storage of blood samples for use in future exploratory pharmacogenetic research.
08 March 2011	Permitted additional safety monitoring of abnormal liver function testing .
14 November 2011	Changes were made to clarify and take into consideration legal guidelines based upon feedback from regulatory agencies and study personnel.
28 February 2014	Addressed the dose selection for the long-term phase of the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported