Clinical trial results:
A Phase 2b, Randomized, Double-Blind, Placebo-Controlled, Dose Ranging, Multi-Center Study to Evaluate the Efficacy and Safety of Clazakizumab Subcutaneous Injection in Adults with Active Psoriatic Arthritis

Revised Protocol 03, incorporating Amendment 05 Pharmacogenetics Blood Sample Amendment 01 - site specific (v1.0, dated 13-Sep-2011)

Summary

EudraCT number	2011-004016-29
Trial protocol	DE HU ES IT CZ
Global end of trial date	18 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	IM133-004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01490450
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	18 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 June 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to characterize the safety, efficacy and dose response of BMS-945429 in subjects with active Psoriatic Arthritis and an inadequate response to NSAIDs and non-biologic DMARDs

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 December 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: 30
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Czechia: 15
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Hungary: 22
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Argentina: 23
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	South Africa: 11
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	165
EEA total number of subjects	87

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)	152
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 275 subjects were enrolled in the study and 165 subjects were randomized o treatment.

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

Arm description:

Subcutaneous, every 4 weeks for 24 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:

Subcutaneous, every 4 weeks for 24 weeks

Arm title	Clazakizumab (25mg)

Arm description:

Subcutaneous, 25 mg, every 4 weeks, for 24 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:

Subcutaneous, every 4 weeks for 24 weeks

Arm title	Clazakizumab (100mg)

Arm description:

Subcutaneous, 100 mg, every 4 weeks, for 24 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:

Subcutaneous, every 4 weeks for 24 weeks

Arm title	Clazakizumab (200mg)
Arm description: Subcutaneous, 200 mg, every 4 weeks, for 24 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: Subcutaneous, every 4 weeks for 24 weeks	

Number of subjects in period 1	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)
Started	41	41	42
Completed	38	40	38
Not completed	3	1	4
No longer met study criteria	-	1	1
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	-	-
Request to discontinue treatment	1	-	-
Lack of efficacy	2	-	3

Number of subjects in period 1	Clazakizumab (200mg)
Started	41
Completed	33
Not completed	8
No longer met study criteria	-
Consent withdrawn by subject	3
Adverse event, non-fatal	5
Request to discontinue treatment	-
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

Arm description:

Subcutaneous, every 4 weeks for 24 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:

Subcutaneous, every 4 weeks for 24 weeks

Arm title	Clazakizumab (25mg)

Arm description:

Subcutaneous, 25 mg, every 4 weeks, for 24 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:

Subcutaneous, every 4 weeks for 24 weeks

Arm title	Clazakizumab (100mg)

Arm description:

Subcutaneous, 100 mg, every 4 weeks, for 24 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:

Subcutaneous, every 4 weeks for 24 weeks

Arm title	Clazakizumab (200mg)

Arm description:

Subcutaneous, 200 mg, every 4 weeks, for 24 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:

Subcutaneous, every 4 weeks for 24 weeks

Number of subjects in period 2[1]	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)
Started	38	40	37
Completed	36	39	37
Not completed	2	1	0
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	1	1	-
Lost to follow-up	-	-	-
Lack of efficacy	-	-	-

Number of subjects in period 2[1]	Clazakizumab (200mg)
Started	32
Completed	28
Not completed	4
Consent withdrawn by subject	-
Adverse event, non-fatal	1
Lost to follow-up	2
Lack of efficacy	1

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
Reporting group description:	
Subcutaneous, every 4 weeks for 24 weeks	
Reporting group title	Clazakizumab (25mg)
Reporting group description:	
Subcutaneous, 25 mg, every 4 weeks, for 24 weeks	
Reporting group title	Clazakizumab (100mg)
Reporting group description:	
Subcutaneous, 100 mg, every 4 weeks, for 24 weeks	
Reporting group title	Clazakizumab (200mg)
Reporting group description:	
Subcutaneous, 200 mg, every 4 weeks, for 24 weeks	

Reporting group values	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)
Number of subjects	41	41	42
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)	38	34	40
From 65-84 years	3	7	2
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	48.0	49.8	49.3
standard deviation	± 10.53	± 14.05	± 10.84
Gender categorical Units: Subjects			
Female	23	23	20
Male	18	18	22

Reporting group values	Clazakizumab (200mg)	Total	
Number of subjects	41	165	
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)	40	152	
From 65-84 years	1	13	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	44.7		
standard deviation	± 13.75	-	
Gender categorical			
Units: Subjects			
Female	20	86	
Male	21	79	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Subcutaneous, every 4 weeks for 24 weeks	
Reporting group title	Clazakizumab (25mg)
Reporting group description: Subcutaneous, 25 mg, every 4 weeks, for 24 weeks	
Reporting group title	Clazakizumab (100mg)
Reporting group description: Subcutaneous, 100 mg, every 4 weeks, for 24 weeks	
Reporting group title	Clazakizumab (200mg)
Reporting group description: Subcutaneous, 200 mg, every 4 weeks, for 24 weeks	
Reporting group title	Placebo
Reporting group description: Subcutaneous, every 4 weeks for 24 weeks	
Reporting group title	Clazakizumab (25mg)
Reporting group description: Subcutaneous, 25 mg, every 4 weeks, for 24 weeks	
Reporting group title	Clazakizumab (100mg)
Reporting group description: Subcutaneous, 100 mg, every 4 weeks, for 24 weeks	
Reporting group title	Clazakizumab (200mg)
Reporting group description: Subcutaneous, 200 mg, every 4 weeks, for 24 weeks	

Primary: Percent of Participants Achieving American College of Rheumatology Criteria 20% Response Rate (ACR20)

End point title	Percent of Participants Achieving American College of Rheumatology Criteria 20% Response Rate (ACR20)[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 16 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	Clazakizumab (25mg)	Clazakizumab (100mg)	Clazakizumab (200mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	41	42	41
Units: percentage of participants				
number (not applicable)	29.3	46.3	52.4	39.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants Achieving Psoriasis Area Severity Index (PASI) 75 Response Rate

End point title	Percent of Participants Achieving Psoriasis Area Severity Index (PASI) 75 Response Rate

End point description:

To calculate the PASI score, the psoriasis plaques found on each body region are graded for their combined redness, thickness, and scaliness. The severity of the plaques in each region is graded on a 0 to 4 scale, with 0 meaning no involvement and 4 meaning severe involvement. Next, the amount of surface area on each body region that is covered by the plaques is calculated. The total surface area affected by psoriasis is graded from 0 to 6, with 0 meaning no involvement and 6 meaning greater than 90 percent of the region covered in plaques.

These grades are then fed into an equation to determine the patient's PASI score. The PASI score then is used as a clinical assessment of the patient's psoriasis involvement. A person free of psoriasis has a score of 0 and the score could be as high as 72.

PASI 75 means that the person's PASI score dropped by 75 percent as a result of the psoriasis treatment.

End point type	Secondary

End point timeframe:

Week 16 and Week 24

End point values	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)	Clazakizumab (200mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	41	42	41
Units: percentage of participants				
number (not applicable)				
week 16	14.6	12.2	16.7	4.9
week 24	12.2	19.5	28.6	12.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants Achieving ACR50 and ACR70 Response Rate

End point title	Percent of Participants Achieving ACR50 and ACR70 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:

Week 16 and Week 24

End point values	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)	Clazakizumab (200mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	41	42	41
Units: percentage of participants				
number (not applicable)				
ACR50 (16 weeks)	7.3	29.3	35.7	17.1
ACR50 (24 weeks)	14.6	34.1	35.7	24.4
ACR70 (16 weeks)	2.4	17.1	14.3	4.9
ACR70 (24 weeks)	4.9	19.5	23.8	12.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants Achieving ACR20 Response Rate at Week 24

End point title	Percent of Participants Achieving ACR20 Response Rate at Week 24

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:

week 24

End point values	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)	Clazakizumab (200mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	41	42	41
Units: percentage of participants				
number (not applicable)	34.1	56.1	57.1	39.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants Achieving a Health Assessment Questionnaire (HAQ) Response

End point title	Percent of Participants Achieving a Health Assessment Questionnaire (HAQ) Response

End point description:

For each item, there is a four-level difficulty scale that is scored from 0 to 3, representing normal (no difficulty) (0), some difficulty (1), much difficulty (2), and unable to do (3). There are 20 questions in eight categories of functioning - dressing, rising, eating, walking, hygiene, reach, grip, and usual activities. The highest component score in each category determines the score for the category, unless aids or devices are required. Dependence on equipment or physical assistance increases a lower score to the level of 2 to more accurately represent underlying disability. The eight category scores are averaged into an overall HAQ score on a scale from zero (no disability) to three (completely disabled). The scale is not truly continuous but has 25 possible values (i.e., 0, 0.125, 0.250, 0.375 … 3).

Response is measured by a reduction of at least 0.3 unit from baseline in HAQ index.

End point type	Secondary

End point timeframe:

Weeks 16 and Week 24

End point values	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)	Clazakizumab (200mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	41	42	41
Units: percentage of participants				
number (not applicable)				
week 16	36.6	48.8	45.2	39.0
week 24	26.8	51.2	47.6	36.6

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline at Week 16 in Short Form (36) [SF-36] Scores

End point title	Mean Change From Baseline at Week 16 in Short Form (36) [SF-36] Scores

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 and Week 16

End point values	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)	Clazakizumab (200mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	40	41	39
Units: score on a scale				
arithmetic mean (standard deviation)				
Mental component	1.4 (± 1.507)	1.2 (± 1.502)	3.7 (± 1.478)	1.1 (± 1.516)
Physical component	4.4 (± 1.236)	6.5 (± 1.236)	4.6 (± 1.217)	4.1 (± 1.248)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline at Week 24 in SF-36 Scores

End point title	Mean Change From Baseline at Week 24 in SF-36 Scores

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 and Week 24

End point values	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)	Clazakizumab (200mg)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	38	36	28
Units: score on a scale				
arithmetic mean (standard deviation)				
Mental component	3.6 (± 1.646)	1.4 (± 1.538)	3.9 (± 1.548)	2.1 (± 1.689)
Physical component	4.9 (± 1.420)	8.2 (± 1.360)	5.7 (± 1.363)	6.4 (± 1.461)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-clazakizumab Antibodies

End point title	Number of Participants With Anti-clazakizumab Antibodies[2]

End point description:

End point type	Secondary

End point timeframe:

Up to 24 weeks

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only arms receiving clazakizumab were reported.

End point values	Clazakizumab (25mg)	Clazakizumab (100mg)	Clazakizumab (200mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	41	42	41	
Units: participants				
number (not applicable)	1	0	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Up to 24 weeks per participant	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0
Reporting groups	
Reporting group title	Placebo
Reporting group description: Subcutaneous, every 4 weeks for 24 weeks	
Reporting group title	Clazakizumab (25mg)
Reporting group description: Subcutaneous, 25 mg, every 4 weeks, for 24 weeks	
Reporting group title	Clazakizumab (100mg)
Reporting group description: Subcutaneous, 100 mg, every 4 weeks, for 24 weeks	
Reporting group title	Clazakizumab (200mg)
Reporting group description: Subcutaneous, 200 mg, every 4 weeks, for 24 weeks	

Serious adverse events	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 41 (4.88%)	2 / 41 (4.88%)	2 / 42 (4.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	0 / 42 (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
Prostate cancer			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	0 / 42 (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
Transitional cell carcinoma			

subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	0 / 42 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	0 / 42 (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
Bradycardia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	0 / 42 (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
Nervous system disorders			
Dystonia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	0 / 42 (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
Hypoaesthesia			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	0 / 42 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	0 / 42 (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
Skin and subcutaneous tissue disorders			
Psoriasis			

subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc disorder			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	0 / 42 (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
Muscular weakness			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	0 / 42 (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 (200mg)		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 41 (9.76%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transitional cell carcinoma			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dystonia			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hemiparesis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoaesthesia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc disorder			

subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Clazakizumab (25mg)	Clazakizumab (100mg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 41 (46.34%)	22 / 41 (53.66%)	20 / 42 (47.62%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 41 (0.00%)	9 / 41 (21.95%)	6 / 42 (14.29%)
occurrences (all)	0	9	6
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 41 (0.00%)	6 / 41 (14.63%)	4 / 42 (9.52%)
occurrences (all)	0	6	4
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 41 (2.44%)	2 / 41 (4.88%)	2 / 42 (4.76%)
occurrences (all)	1	2	2
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 41 (9.76%)	3 / 41 (7.32%)	2 / 42 (4.76%)
occurrences (all)	4	3	2
Migraine			
subjects affected / exposed	3 / 41 (7.32%)	0 / 41 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
General disorders and administration			

site conditions			
Injection site erythema			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	3 / 42 (7.14%)
occurrences (all)	0	0	3
Injection site reaction			
subjects affected / exposed	1 / 41 (2.44%)	4 / 41 (9.76%)	1 / 42 (2.38%)
occurrences (all)	1	4	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 41 (4.88%)	1 / 41 (2.44%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Gastritis			
subjects affected / exposed	1 / 41 (2.44%)	4 / 41 (9.76%)	0 / 42 (0.00%)
occurrences (all)	1	4	0
Nausea			
subjects affected / exposed	3 / 41 (7.32%)	0 / 41 (0.00%)	1 / 42 (2.38%)
occurrences (all)	3	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 41 (4.88%)	0 / 41 (0.00%)	3 / 42 (7.14%)
occurrences (all)	2	0	3
Nasopharyngitis			
subjects affected / exposed	1 / 41 (2.44%)	6 / 41 (14.63%)	2 / 42 (4.76%)
occurrences (all)	1	6	2
Pharyngitis			
subjects affected / exposed	4 / 41 (9.76%)	4 / 41 (9.76%)	1 / 42 (2.38%)
occurrences (all)	4	4	1
Upper respiratory tract infection			
subjects affected / exposed	6 / 41 (14.63%)	0 / 41 (0.00%)	3 / 42 (7.14%)
occurrences (all)	6	0	3
Urinary tract infection			
subjects affected / exposed	2 / 41 (4.88%)	4 / 41 (9.76%)	1 / 42 (2.38%)
occurrences (all)	2	4	1
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 41 (0.00%)	5 / 41 (12.20%)	2 / 42 (4.76%)
occurrences (all)	0	5	2

Hyperlipidaemia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	3 / 42 (7.14%)
occurrences (all)	0	1	3

Non-serious adverse events	Clazakizumab (200mg)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 41 (65.85%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 41 (19.51%)		
occurrences (all)	8		
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	0 / 41 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Injection site reaction			
subjects affected / exposed	2 / 41 (4.88%)		
occurrences (all)	2		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all) Gastritis subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	3 / 41 (7.32%) 3 1 / 41 (2.44%) 1 1 / 41 (2.44%) 1		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 1 / 41 (2.44%) 1 4 / 41 (9.76%) 4 1 / 41 (2.44%) 1 1 / 41 (2.44%) 1 0 / 41 (0.00%) 0		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all) Hyperlipidaemia subjects affected / exposed occurrences (all)	 5 / 41 (12.20%) 5 0 / 41 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 September 2011	To permit the collection and storage of blood samples for use in future exploratory pharmacogenetic research.
26 June 2012	-To modify the study design to address a concern from the FDA that a small percentage of DMARD-IR/NSAID-IR PsA subjects who may be randomized to pure placebo and, therefore, not receive any active treatment which may potentially put subjects with high disease activity at risk for structural damage. -To require that all subjects planning to participate be on stable background methotrexate therapy prior to randomization.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported