



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 standard deviation | 49.9 ± 13.95 | 50.0 ± 12.53 | 46.4 ± 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 standard deviation | 52.8 ± 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 (\pm 1.271) | 8.0 (\pm 1.219) | 7.1 (\pm 1.246) | |
| Physical component (week 12) | 6.8 (\pm 1.028) | 7.3 (\pm 0.994) | 8.4 (\pm 1.006) | |
| Physical component (week 24) | 7.7 (\pm 1.094) | 8.2 (\pm 1.057) | 8.2 (\pm 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 (\pm 3.146) | -20.8 (\pm 3.060) | -19.4 (\pm 3.077) | -27.4 (\pm 3.077) |
| week 24 | -12.9 (\pm 3.306) | -23.9 (\pm 3.052) | -22.3 (\pm 3.131) | -31.3 (\pm 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 (\pm 3.180) | -18.6 (\pm 3.056) | -26.3 (\pm 3.080) | |
| week 24 | -17.7 (\pm 3.184) | -23.4 (\pm 3.056) | -27.0 (\pm 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 yields four types of scores:

1. Absenteeism (work time missed)

2. Presenteeism (impairment at work / reduced on-the-job effectiveness)

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

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

| | | | |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 4 / 61 (6.56%) 4 | 2 / 59 (3.39%) 2 | 3 / 60 (5.00%) 3 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 7 / 61 (11.48%) 7 | 5 / 59 (8.47%) 5 | 1 / 60 (1.67%) 1 |
| Pharyngitis subjects affected / exposed occurrences (all) | 5 / 61 (8.20%) 5 | 2 / 59 (3.39%) 2 | 3 / 60 (5.00%) 3 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 4 / 61 (6.56%) 4 | 5 / 59 (8.47%) 5 | 1 / 60 (1.67%) 1 |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 61 (0.00%) 0 | 1 / 59 (1.69%) 1 | 2 / 60 (3.33%) 2 |
| Herpes zoster subjects affected / exposed occurrences (all) | 0 / 61 (0.00%) 0 | 1 / 59 (1.69%) 1 | 1 / 60 (1.67%) 1 |
| Metabolism and nutrition disorders | | | |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 2 / 61 (3.28%) 2 | 7 / 59 (11.86%) 7 | 7 / 60 (11.67%) 7 |
| Dyslipidaemia subjects affected / exposed occurrences (all) | 1 / 61 (1.64%) 1 | 7 / 59 (11.86%) 7 | 4 / 60 (6.67%) 4 |
| Hypertriglyceridaemia subjects affected / exposed occurrences (all) | 2 / 61 (3.28%) 2 | 1 / 59 (1.69%) 1 | 1 / 60 (1.67%) 1 |
| Hyperlipidaemia subjects affected / exposed occurrences (all) | 0 / 61 (0.00%) 0 | 3 / 59 (5.08%) 3 | 0 / 60 (0.00%) 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 occurrences (all) | 13 / 60 (21.67%) 13 | 1 / 59 (1.69%) 1 | 1 / 60 (1.67%) 1 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 14 / 60 (23.33%) 14 | 0 / 59 (0.00%) 0 | 12 / 60 (20.00%) 12 |
| Gamma-glutamyl transferease increased subjects affected / exposed occurrences (all) | 4 / 60 (6.67%) 4 | 0 / 59 (0.00%) 0 | 2 / 60 (3.33%) 2 |
| Injury, poisoning and procedural complications | | | |
| Arthropod bite subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | 0 / 59 (0.00%) 0 | 1 / 60 (1.67%) 1 |
| Overdose subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 3 / 59 (5.08%) 3 | 0 / 60 (0.00%) 0 |
| Vascular disorders | | | |
| Hypertension subjects affected / exposed occurrences (all) | 4 / 60 (6.67%) 4 | 6 / 59 (10.17%) 6 | 2 / 60 (3.33%) 2 |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 59 (1.69%) 1 | 2 / 60 (3.33%) 2 |
| General disorders and administration site conditions | | | |
| Injection site reaction subjects affected / exposed occurrences (all) | 11 / 60 (18.33%) 11 | 14 / 59 (23.73%) 14 | 9 / 60 (15.00%) 9 |
| Ejection site erythema subjects affected / exposed occurrences (all) | 15 / 60 (25.00%) 15 | 10 / 59 (16.95%) 10 | 9 / 60 (15.00%) 9 |
| Injection site rash subjects affected / exposed occurrences (all) | 8 / 60 (13.33%) 8 | 2 / 59 (3.39%) 2 | 8 / 60 (13.33%) 8 |
| Injection site dermatitis | | | |

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

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | 1 / 59 (1.69%) 1 | 0 / 60 (0.00%) 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) | 2 / 59 (3.39%) 2 | | |
| Leukopenia subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 6 / 59 (10.17%) 6 | | |
| Nausea subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | | |
| Dyspepsia subjects affected / exposed occurrences (all) | 3 / 59 (5.08%) 3 | | |
| Skin and subcutaneous tissue disorders Dermatitis allergic subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | | |
| Skin lesion subjects affected / exposed occurrences (all) | 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) | 2 / 59 (3.39%) 2 | | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 59 (0.00%) 0 | | |
| Pharyngitis | | | |

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

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