



Clinical trial results:

A PHASE 3 RANDOMIZED PLACEBO CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF ABATACEPT SUBCUTANEOUS INJECTION IN ADULTS WITH ACTIVE PSORIATIC ARTHRITIS

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2012-002798-80 |
| Trial protocol | ES DE GR IT CZ PL FR |
| Global end of trial date | 30 June 2020 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 16 July 2021 |
| First version publication date | 16 July 2021 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | IM101-332 |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Bristol-Myers Squibb |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170 |
| Public contact | EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com |
| Scientific contact | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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 | 16 November 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 June 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of abatacept to placebo as assessed by the ACR20 response at Day 169

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 05 June 2013 |
| 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 | Argentina: 44 |
| Country: Number of subjects enrolled | Brazil: 16 |
| Country: Number of subjects enrolled | Canada: 5 |
| Country: Number of subjects enrolled | Chile: 39 |
| Country: Number of subjects enrolled | Colombia: 14 |
| Country: Number of subjects enrolled | Czechia: 14 |
| Country: Number of subjects enrolled | France: 19 |
| Country: Number of subjects enrolled | Germany: 22 |
| Country: Number of subjects enrolled | Greece: 6 |
| Country: Number of subjects enrolled | Israel: 18 |
| Country: Number of subjects enrolled | Italy: 23 |
| Country: Number of subjects enrolled | Mexico: 66 |
| Country: Number of subjects enrolled | Peru: 15 |
| Country: Number of subjects enrolled | Poland: 18 |
| Country: Number of subjects enrolled | South Africa: 39 |
| Country: Number of subjects enrolled | Spain: 31 |
| Country: Number of subjects enrolled | United States: 100 |
| Worldwide total number of subjects | 489 |
| EEA total number of subjects | 133 |

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) | 439 |
| From 65 to 84 years | 50 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

424 Were Randomized and Treated

Period 1

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|-----------|
| Arm title | Abatacept |
|------------------|-----------|

Arm description:

Abatacept 125mg, self-administered subcutaneously, once weekly

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

Dosage and administration details:

125 mg/mL

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Placebo, self-administered subcutaneously, once weekly.

| | |
|--|------------------------|
| 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:

125mg/syringe

| Number of subjects in period 1^[1] | Abatacept | Placebo |
|---|-----------|---------|
| Started | 213 | 211 |
| Completed | 125 | 98 |
| Not completed | 88 | 113 |
| Subject request to discontinue treatment | 2 | 3 |

| | | |
|---|----|----|
| Consent withdrawn by subject | 3 | 5 |
| Adverse event, non-fatal | 1 | 3 |
| Early Escape: Transitioned to OL period | 76 | 89 |
| Entered Open-Label in error | - | 1 |
| Subject no longer met criteria | 1 | - |
| Lack of efficacy | 5 | 12 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 424 participants were randomized and treated

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Open-Label |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | No |
| Arm title | Abatacept |

Arm description:

Abatacept 125mg, self-administered subcutaneously, once weekly

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

Dosage and administration details:

125mg/mL

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Placebo, self-administered subcutaneously, once weekly.

| | |
|--|------------------------|
| 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:

125mg/syringe

| Number of subjects in period 2 | Abatacept | Placebo |
|--|-----------|---------|
| Started | 197 | 185 |
| Completed | 123 | 121 |
| Not completed | 74 | 64 |
| Consent withdrawn by subject | 4 | 1 |
| Adverse event, non-fatal | 2 | 4 |
| Other Reasons | 1 | 1 |
| Subject request discontinue treatment | 4 | 3 |
| Lost to follow-up | 1 | 2 |
| Ongoing OL treatment at time of analysis | 46 | 45 |
| Lack of efficacy | 16 | 8 |

Period 3

| | |
|------------------------------|-------------------------|
| Period 3 title | Long Term Extension |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | No |
| Arm title | Abatacept |

Arm description:

Abatacept 125mg, self-administered subcutaneously, once weekly

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

Dosage and administration details:

125mg/mL

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Placebo, self-administered subcutaneously, once weekly.

| | |
|--|------------------------|
| 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:

125mg/syringe

| Number of subjects in period 3 | Abatacept | Placebo |
|--|-----------|---------|
| Started | 113 | 115 |
| Completed | 0 | 8 |
| Not completed | 113 | 107 |
| Subject request to discontinue treatment | 2 | - |
| Consent withdrawn by subject | 1 | - |
| Adverse event, non-fatal | 1 | - |
| Ongoing treatment at time of analysis | 106 | 100 |
| Lack of efficacy | 3 | 7 |

Baseline characteristics

Reporting groups

| | |
|--|-----------|
| Reporting group title | Abatacept |
| Reporting group description: Abatacept 125mg, self-administered subcutaneously, once weekly | |
| Reporting group title | Placebo |
| Reporting group description: Placebo, self-administered subcutaneously, once weekly. | |

| Reporting group values | Abatacept | Placebo | Total |
|---|-----------|---------|-------|
| Number of subjects | 213 | 211 | 424 |
| Age categorical Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 51.0 | 49.8 | |
| standard deviation | ± 10.67 | ± 11.26 | - |
| Sex: Female, Male Units: | | | |
| Female | 121 | 112 | 233 |
| Male | 92 | 99 | 191 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 1 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 |
| White | 195 | 198 | 393 |
| More than one race | 18 | 11 | 29 |
| Unknown or Not Reported | 0 | 1 | 1 |

End points

End points reporting groups

| | |
|--|-----------|
| Reporting group title | Abatacept |
| Reporting group description: Abatacept 125mg, self-administered subcutaneously, once weekly | |
| Reporting group title | Placebo |
| Reporting group description: Placebo, self-administered subcutaneously, once weekly. | |
| Reporting group title | Abatacept |
| Reporting group description: Abatacept 125mg, self-administered subcutaneously, once weekly | |
| Reporting group title | Placebo |
| Reporting group description: Placebo, self-administered subcutaneously, once weekly. | |
| Reporting group title | Abatacept |
| Reporting group description: Abatacept 125mg, self-administered subcutaneously, once weekly | |
| Reporting group title | Placebo |
| Reporting group description: Placebo, self-administered subcutaneously, once weekly. | |

Primary: Proportion of ACR 20 Responders at Day 169

| | |
|--|--|
| End point title | Proportion of ACR 20 Responders at Day 169 |
| End point description: The American College of Rheumatology (ACR) 20 definition of improvement is a 20% improvement over baseline in tender and swollen joint counts and a 20% improvement in 3 of the 5 remaining core data set measures (participant global assessment of pain, participant global assessment of disease activity, physician global assessment of disease activity, participant assessment of physical function, acute phase reactant value). The number of ACR 20 responders was divided by the number of treated participants and expressed as a percentage. Early escape participants, and participants with missing data at day 169 were imputed as non-responders. | |
| End point type | Primary |
| End point timeframe: Day 169 | |

| End point values | Abatacept | Placebo | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 211 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 39.4 (32.9 to 46.0) | 22.3 (16.7 to 27.9) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | SA of Proportion of ACR 20 Responders at day 169 |
| Comparison groups | Abatacept v Placebo |
| Number of subjects included in analysis | 424 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Estimate of Difference |
| Point estimate | 17.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8.7 |
| upper limit | 25.6 |

Secondary: Proportion of Health Assessment Questionnaire (HAQ) responders at Day 169

| | |
|-----------------|---|
| End point title | Proportion of Health Assessment Questionnaire (HAQ) responders at Day 169 |
|-----------------|---|

End point description:

Participants were considered responders if their HAQ score decreased at least 0.35 from baseline. The number of HAQ responders was divided by the number of treated participants and expressed as a percentage. Scoring conventions are based on the Standard Disability Index of HAQ/HAQ-DI using the 20 response items. For each of the 8 disability categories there is an "aids/devices" companion variable that is used to record the type of assistance, if any, a participant uses for his/her usual activities. If either "aids/devices" and/or "assistance from another person" are checked for a disability category, the score for this category is set to "2" (much difficulty), if the original score was "0" (no difficulty) or "1" (some difficulty). The HAQ-DI is then calculated by summing the adjusted categories scores and dividing by the number of categories answered. Early escape participants, and participants with missing data at day 169 were imputed as non-responders.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Day 169

| | | | | |
|-----------------------------------|---------------------|---------------------|--|--|
| End point values | Abatacept | Placebo | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 211 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 31.0 (24.8 to 37.2) | 23.7 (18.0 to 29.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of ACR 20 responders at Day 169 in the TNFi-naïve

subpopulation

| | |
|-----------------|--|
| End point title | Proportion of ACR 20 responders at Day 169 in the TNFi-naïve subpopulation |
|-----------------|--|

End point description:

The ACR 20 definition of improvement is a 20% improvement over baseline in tender and swollen joint counts and a 20% in 3 of the 5 remaining core data set measures (participant global assessment of pain, participant global assessment of disease activity, physician global assessment of disease activity, participant assessment of physical function, acute phase reactant value). The number of ACR 20 responders was divided by the number of treated, TNFi-naïve participants and expressed as a percentage. Early escape participants, and participants with missing data at day 169 were imputed as non-responders.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 169

| End point values | Abatacept | Placebo | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 84 | 81 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 44.0 (33.4 to 54.7) | 22.2 (13.2 to 31.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of ACR 20 responders at Day 169 in the TNFi-exposed subpopulation

| | |
|-----------------|--|
| End point title | Proportion of ACR 20 responders at Day 169 in the TNFi-exposed subpopulation |
|-----------------|--|

End point description:

The ACR 20 definition of improvement is a 20% improvement over baseline in tender and swollen joint counts and a 20% in 3 of the 5 remaining core data set measures (participant global assessment of pain, participant global assessment of disease activity, physician global assessment of disease activity, participant assessment of physical function, acute phase reactant value). The number of ACR 20 responders was divided by the number of treated, TNFi-exposed participants and expressed as a percentage. Early escape participants, and participants with missing data at day 169 were imputed as non-responders.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 169

| End point values | Abatacept | Placebo | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 129 | 130 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 36.4 (28.1 to 44.7) | 22.3 (15.2 to 29.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of non-progressors in total PsA-modified SHS at Day 169

| | |
|--|--|
| End point title | Proportion of non-progressors in total PsA-modified SHS at Day 169 |
| End point description: | |
| The number of radiographic non-progressors in total PsA-Modified Sharp van der Heijde score (SHS) at Day 169 was divided by the number of treated participants and expressed as a percentage. Non-progression was defined as a change from baseline in total PsA modified SHS ≤ 0 . Early escape participants, and participants with missing data at day 169 were imputed as non-progressors. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Day 169 | |

| End point values | Abatacept | Placebo | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 211 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 42.7 (36.1 to 49.4) | 32.7 (26.4 to 39.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants achieving a PASI 50 at Day 169 in participants with baseline BSA $\geq 3\%$

| | |
|--|--|
| End point title | Proportion of participants achieving a PASI 50 at Day 169 in participants with baseline BSA $\geq 3\%$ |
| End point description: | |
| The number of participants who achieved at least 50% improvement from baseline in Psoriasis Area and Severity Index Arthritis (PASI 50) at Day 169 was divided by the number of treated participants with BSA $\geq 3\%$ and expressed as a percentage. Only participants with $\geq 3\%$ body surface area (BSA) of psoriatic skin involvement at randomization were included in this analysis. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Day 169 | |

| End point values | Abatacept | Placebo | | |
|-----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 146 | 148 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 26.7 (19.5 to 33.9) | 19.6 (13.2 to 26.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportions of ACR 50 and ACR 70 responders at Day 169

| | |
|--|--|
| End point title | Proportions of ACR 50 and ACR 70 responders at Day 169 |
| End point description: | |
| The ACR 50 and ACR 70 definition of improvement is a 50% or 70% improvement, respectively, over baseline in tender and swollen joint counts and a 50% or 70% improvement in 3 of the 5 remaining core data set measures (participant global assessment of pain, participant global assessment of disease activity, physician global assessment of disease activity, participant assessment of physical function, acute phase reactant value). The number of ACR 50 and ACR 70 responders was divided by the number of treated participants and expressed as a percentage. Early escape participants, and participants with missing data at day 169 were imputed as non-responders. | |
| End point type | Secondary |
| End point timeframe: | |
| Day 169 | |

| End point values | Abatacept | Placebo | | |
|-----------------------------------|---------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 211 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| ACR 50 | 19.2 (14.0 to 24.5) | 12.3 (7.9 to 16.8) | | |
| ACR 70 | 10.3 (6.2 to 14.4) | 6.6 (3.3 to 10.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline in SF-36 physical and mental components at Day 169

| | |
|-----------------|--|
| End point title | Mean change from baseline in SF-36 physical and mental |
|-----------------|--|

End point description:

Adjusted mean change in scores on the Short Form 36 physical and mental function assessment (SF-36) from baseline were analyzed from the physical component summary (PCS) mental component summary (MCS). The SF-36 is a participant questionnaire assessing 8 domains of health status: physical functioning, pain, vitality, social functioning, psychological functioning, general health perception, and role limitations due to physical and emotional problems. The instrument can be divided into two summary scores, physical and mental component score. The scores range from 0 to 100, with a higher score indicating better quality of life. The two summary scores (PCS and MCS) will be calculated by taking a weighted linear combination of the 8 individual subscales.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Day 169

| End point values | Abatacept | Placebo | | |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 211 | | |
| Units: SF-36 points | | | | |
| arithmetic mean (standard error) | | | | |
| PCS | 5.11 (± 0.637) | 3.69 (± 0.707) | | |
| MCS | 2.56 (± 0.826) | 2.62 (± 0.924) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with at least one positive immunogenicity response up to Day 169 relative to baseline

| | |
|-----------------|--|
| End point title | Proportion of participants with at least one positive immunogenicity response up to Day 169 relative to baseline |
|-----------------|--|

End point description:

Blood samples were collected at Days 1, 85 and 169 and assayed for the presence of abatacept-specific antibodies. The number of participants with at least one positive immunogenicity response was divided by the number of treated participants and expressed as a percentage.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Day 169

| End point values | Abatacept | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 203 | 198 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 3.9 | 8.6 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with AEs at Day 169

| | |
|--|--|
| End point title | Proportion of participants with AEs at Day 169 |
| End point description: Proportion of participants with AEs at Day 169 | |
| End point type | Secondary |
| End point timeframe: Day 169 | |

| End point values | Abatacept | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 211 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 54.5 | 53.1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with SAEs at Day 169

| | |
|---|---|
| End point title | Proportion of participants with SAEs at Day 169 |
| End point description: Proportion of participants with SAEs at Day 169 | |
| End point type | Secondary |
| End point timeframe: Day 169 | |

| End point values | Abatacept | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 211 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 2.8 | 4.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with AEs leading to discontinuation at Day 169

| | |
|-----------------|---|
| End point title | Proportion of participants with AEs leading to discontinuation at Day 169 |
|-----------------|---|

End point description:

Proportion of participants with AEs leading to discontinuation at Day 169

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 169

| End point values | Abatacept | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 211 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 1.4 | 1.9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participant deaths at Day 169

| | |
|-----------------|---|
| End point title | Proportion of participant deaths at Day 169 |
|-----------------|---|

End point description:

Proportion of participant deaths at Day 169

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 169

| End point values | Abatacept | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 211 | | |
| Units: Percentage of participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of participants with marked laboratory abnormalities at Day 169

| | |
|------------------------|--|
| End point title | Proportion of participants with marked laboratory abnormalities at Day 169 |
| End point description: | Proportion of participants with marked laboratory abnormalities at Day 169 |
| End point type | Secondary |
| End point timeframe: | Day 169 |

| End point values | Abatacept | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 213 | 211 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 3.2 | 5.4 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All reported AEs including those that occur more than 56 days after the last dose of study medication

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------------------|
| Reporting group title | ABATACEPT DURING DOUBLE-BLIND PERIOD |
|-----------------------|--------------------------------------|

Reporting group description:

Subject self-administered 125 mg/syringe (125 mg/mL) of Abatacept subcutaneously(SC) once weekly for 24 weeks.

| | |
|-----------------------|------------------------------------|
| Reporting group title | PLACEBO DURING DOUBLE-BLIND PERIOD |
|-----------------------|------------------------------------|

Reporting group description:

Subject self-administered 125 mg/syringe Placebo matching Abatacept SC once weekly for 24 weeks.

| | |
|-----------------------|------------------------------------|
| Reporting group title | ABATACEPT DURING OPEN-LABEL PERIOD |
|-----------------------|------------------------------------|

Reporting group description:

All subjects transitioned to the Open-label Period and self-administered 125 mg/syringe (125 mg/mL) of Abatacept subcutaneously (SC) once weekly for 28 weeks.

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| Reporting group title | ABATACEPT DURING OPEN-LABEL EXTENSION PERIOD |
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Reporting group description:

Subjects self-administered 125 mg/syringe (125 mg/mL) of Abatacept subcutaneously (SC) once weekly during the open label extension period.

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|-----------------------|---|
| Reporting group title | ABATACEPT DURING LONG-TERM EXTENSION PERIOD |
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Reporting group description:

At the end of Open-label Period, subjects entered a one-year, Long-term Extension Period during which only safety data was collected. The protocol was then extended for an additional 3 years in 6 countries in compliance with local regulatory requirements. Subjects self-administered 125 mg/syringe (125 mg/mL) of Abatacept subcutaneously (SC) once weekly.

| Serious adverse events | ABATACEPT DURING DOUBLE-BLIND PERIOD | PLACEBO DURING DOUBLE-BLIND PERIOD | ABATACEPT DURING OPEN-LABEL PERIOD |
|---|--------------------------------------|------------------------------------|------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 213 (2.82%) | 9 / 211 (4.27%) | 29 / 382 (7.59%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 0 / 382 (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 |
| Invasive ductal breast carcinoma | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 0 / 382 (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 |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Carcinoma in situ of skin | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Parathyroid tumour benign | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transitional cell carcinoma | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine leiomyoma | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Peripheral artery thrombosis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 0 / 382 (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 |
| Venous thrombosis | | | |
| subjects affected / exposed | 1 / 213 (0.47%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Incarcerated hernia | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 0 / 382 (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 |
| Reproductive system and breast disorders | | | |
| Polycystic ovaries | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute chest syndrome | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 0 / 382 (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 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 213 (0.47%) | 0 / 211 (0.00%) | 0 / 382 (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 embolism | | | |
| subjects affected / exposed | 1 / 213 (0.47%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 0 / 382 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Vascular pseudoaneurysm | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 0 / 382 (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 |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Fall | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Meniscus injury | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Patella fracture | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Congenital, familial and genetic disorders | | | |
| Dermoid cyst | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| 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 | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Demyelination | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Transient ischaemic attack | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 0 / 382 (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 |
| Ear and labyrinth disorders | | | |
| Meniere's disease | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| 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 pain | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Colitis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric mucosa erythema | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive pancreatitis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary dilatation | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic fibrosis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Erythrodermic psoriasis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Psoriasis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Calculus bladder | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 213 (0.47%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Psoriatic arthropathy | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 2 / 382 (0.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chondropathy | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metatarsalgia | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 1 / 211 (0.47%) | 0 / 382 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 213 (0.94%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Pneumocystis jirovecii infection | | | |
| subjects affected / exposed | 1 / 213 (0.47%) | 0 / 211 (0.00%) | 0 / 382 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Epstein-Barr virus infection | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Groin abscess | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Intervertebral discitis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 0 / 211 (0.00%) | 0 / 382 (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 | ABATACEPT DURING OPEN-LABEL EXTENSION PERIOD | ABATACEPT DURING LONG-TERM EXTENSION PERIOD | |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 20 / 322 (6.21%) | 17 / 106 (16.04%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carcinoma in situ of skin | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parathyroid tumour benign | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| Transitional cell carcinoma subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine leiomyoma subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders Peripheral artery thrombosis subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous thrombosis subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions Chest pain subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incarcerated hernia subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders Anaphylactic reaction subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders Polycystic ovaries | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute chest syndrome | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Vascular pseudoaneurysm | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Accidental overdose | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscus injury | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Patella fracture | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Dermoid cyst | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Nervous system disorders | | | |
| Demyelination | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Meniere's disease | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric mucosa erythema | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obstructive pancreatitis | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary dilatation | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic fibrosis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Erythrodermic psoriasis | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Calculus bladder | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psoriatic arthropathy | | | |
| subjects affected / exposed | 3 / 322 (0.93%) | 3 / 106 (2.83%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chondropathy | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metatarsalgia | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 4 / 322 (1.24%) | 2 / 106 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis | | | |
| subjects affected / exposed | 2 / 322 (0.62%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis jirovecii infection | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epstein-Barr virus infection | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Groin abscess | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral discitis | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 322 (0.00%) | 0 / 106 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth abscess | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 322 (0.00%) | 1 / 106 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | ABATACEPT DURING DOUBLE-BLIND PERIOD | PLACEBO DURING DOUBLE-BLIND PERIOD | ABATACEPT DURING OPEN-LABEL PERIOD |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 46 / 213 (21.60%) | 47 / 211 (22.27%) | 106 / 382 (27.75%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 5 / 213 (2.35%) | 8 / 211 (3.79%) | 10 / 382 (2.62%) |
| occurrences (all) | 5 | 8 | 11 |
| Nervous system disorders | | | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 213 (0.47%) | 0 / 211 (0.00%) | 2 / 382 (0.52%) |
| occurrences (all) | 1 | 0 | 2 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Catarrh | | | |
| subjects affected / exposed | 1 / 213 (0.47%) | 0 / 211 (0.00%) | 1 / 382 (0.26%) |
| occurrences (all) | 1 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 4 / 213 (1.88%) | 2 / 211 (0.95%) | 10 / 382 (2.62%) |
| occurrences (all) | 4 | 2 | 10 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 9 / 213 (4.23%) | 11 / 211 (5.21%) | 17 / 382 (4.45%) |
| occurrences (all) | 11 | 12 | 19 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 6 / 213 (2.82%) | 14 / 211 (6.64%) | 23 / 382 (6.02%) |
| occurrences (all) | 7 | 15 | 28 |
| Bronchitis | | | |
| subjects affected / exposed | 7 / 213 (3.29%) | 5 / 211 (2.37%) | 19 / 382 (4.97%) |
| occurrences (all) | 8 | 5 | 20 |

| | | | |
|-----------------------------|------------------|-----------------|------------------|
| Influenza | | | |
| subjects affected / exposed | 4 / 213 (1.88%) | 3 / 211 (1.42%) | 9 / 382 (2.36%) |
| occurrences (all) | 4 | 3 | 11 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 213 (0.00%) | 2 / 211 (0.95%) | 5 / 382 (1.31%) |
| occurrences (all) | 0 | 2 | 5 |
| Urinary tract infection | | | |
| subjects affected / exposed | 10 / 213 (4.69%) | 2 / 211 (0.95%) | 10 / 382 (2.62%) |
| occurrences (all) | 12 | 2 | 11 |

| Non-serious adverse events | ABATACEPT DURING OPEN-LABEL EXTENSION PERIOD | ABATACEPT DURING LONG-TERM EXTENSION PERIOD | |
|---|--|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 122 / 322 (37.89%) | 90 / 106 (84.91%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 7 / 322 (2.17%) | 9 / 106 (8.49%) | |
| occurrences (all) | 8 | 10 | |
| Nervous system disorders | | | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 322 (0.31%) | 6 / 106 (5.66%) | |
| occurrences (all) | 1 | 7 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Catarrh | | | |
| subjects affected / exposed | 2 / 322 (0.62%) | 12 / 106 (11.32%) | |
| occurrences (all) | 2 | 17 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 11 / 322 (3.42%) | 12 / 106 (11.32%) | |
| occurrences (all) | 11 | 20 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 26 / 322 (8.07%) | 16 / 106 (15.09%) | |
| occurrences (all) | 32 | 24 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 19 / 322 (5.90%) | 3 / 106 (2.83%) | |
| occurrences (all) | 20 | 6 | |

| | | | |
|-----------------------------|------------------|-------------------|--|
| Bronchitis | | | |
| subjects affected / exposed | 17 / 322 (5.28%) | 15 / 106 (14.15%) | |
| occurrences (all) | 19 | 18 | |
| Influenza | | | |
| subjects affected / exposed | 17 / 322 (5.28%) | 4 / 106 (3.77%) | |
| occurrences (all) | 18 | 4 | |
| Pharyngitis | | | |
| subjects affected / exposed | 10 / 322 (3.11%) | 6 / 106 (5.66%) | |
| occurrences (all) | 12 | 6 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 12 / 322 (3.73%) | 8 / 106 (7.55%) | |
| occurrences (all) | 13 | 9 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 22 July 2013 | <p>Changed "entering" to "continue into" when describing how subjects can continue the one year long term extension (Section 3.1.4).</p> <p>Added azathioprine as a medication which must be discontinued 28 days or five half lives prior to randomization.</p> <p>Deleted study from the breast cancer screening exclusion.</p> <p>Added "prior to randomization (Day 1) to exclusions from Medical History Exclusion Criteria n, q, and v [Section 3.3.2, Subsection 2)].</p> <p>Added an exclusion for treatment with phototherapy within 28 days prior to randomization and hypersensitivity to investigational product excipients.</p> <p>Added that the target lesion must not be in the axilla, genitals, groins, palms, or soles.</p> <p>Changed dose reduction to dose limitation in the definition of intolerance for prior use of DMARDs.</p> <p>Changed information on methods of contraception based on new language currently in discussion (protocol body and Appendix 2).</p> <p>Clarified criteria for missed doses requiring discontinuation of treatment to be consistent throughout the protocol.</p> <p>Added that subjects should avoid taking MTX within 48 hours of study drug administration to simplify determination of relatedness of adverse events to the study drug.</p> |
| 22 July 2013 | <p>Added the hyaluronic acid is not permitted in the double-blind and open label periods.</p> <p>Added storage conditions for investigational drug in the Study Treatment section.</p> <p>Changed procedure guide to instructions to describe how subjects will be trained in the use of the safety syringe.</p> <p>Changed caretaker to caregiver in Section 4.3 to be consistent with other language in the protocol.</p> <p>Added immunogenicity to information for which the BMS Bioanalytical Science Department or designee will be unblinded.</p> <p>Added note that the Physician and Subject Global Assessments if Disease Activity refers to arthritis as the disease (Table 5.1-2, Table 5.1-3, and Section 5.4.4.)</p> <p>Added note that subjects should not apply emollients to the skin on the day of their office visits (Table 5.1-2, Table 5.1-3, and Section 5.4.4).</p> <p>Changed description of OL-1 to correctly refer to "Same day as final day in the Double Blind Period.</p> <p>Deleted urine pregnancy test in OL-1 since the testing is already done on the last day in the double blind period.</p> <p>Corrected table note references for Dosing Injectable Study Medication in Table 5.1-3.</p> <p>Added into table notes regarding provisioning of urine pregnancy</p> |

| | |
|-----------------|---|
| 29 October 2013 | <p>Modified definition of menopause to be 12 months amenorrhea rather than 6 months.</p> <p>Added prior treatment of briakinumab as an exclusion criteria.</p> <p>Indicated the Target Lesion should be assessed in addition to be identified at screening.</p> <p>Added window the Day 1 radiograph to be - 3 days.</p> <p>Corrected PK/PD substudy flow chart to delete information indicating a PK sample is collected at Day 169.</p> <p>Clarified that the clinical assessor for enthesitis, dactylitis, PASI, target lesion, and physician visual analog scales may be a different person from the joint assessor.</p> <p>Added a window for the biopsy sample collection to be - 3 days on Days 1 and 169.</p> <p>Clarified when pregnancy tests are required.</p> <p>Corrected PK table 5.5.1-1 to add sample collection and testing at Early Termination in the double-blind period.</p> |
| 19 August 2014 | <p>Changed screening period from 7-42 to 7-56 days.</p> <p>Added permission for rescreening.</p> <p>Modified inclusion criteria for target lesion to be at screening and randomization/Day 1.</p> <p>Changed exclusion criteria for subjects who have been exposed to more than 2 TNFi to specify subjects who have failed more than 2 TNFi due to inefficacy.</p> <p>Changed drug stabilization time for prior use of TNFis.</p> <p>Deleted exclusion of prior use of apremilast, ustekinumab, and briakinumab.</p> <p>Added drug stabilization time for prior use of apremilast, ustekinumab, and briakinumab.</p> <p>Changed TB testing to allow use of a gamma release assay.</p> |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported