# Clinical trial results:
# A Phase 2b, Dose-ranging Study to Evaluate the Efficacy and Safety of Sifalimumab in Adults with Systemic Lupus Erythematosus

## Summary

| | |
|---|---|
| EudraCT number | 2010-024069-30 |
| Trial protocol | NL GB HU ES DE IT BG |
| Global end of trial date | 17 April 2014 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 08 May 2016 |
| First version publication date | 12 August 2015 |
| Version creation reason | |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CD-IA-MEDI-545-1067 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01283139 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | AstraZeneca AB |
| Sponsor organisation address | SE-151 85, Södertälje, Sweden, |
| Public contact | Gabor Illei, MD, Senior Director,Clinical development, AstraZeneca AB, IlleiG@Medimmune.com |
| Scientific contact | Gabor Illei, MD, Senior Director,Clinical development, AstraZeneca AB, IlleiG@Medimmune.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 | 17 April 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 17 April 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of sifalimumab compared to placebo in participants with chronic, moderately-to-severely active Systemic Lupus Erythematosus (SLE) with an inadequate response to standard of care (SOC) for SLE on Day 365 (Week 52).

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating participant signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 31 March 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Argentina: 20 |
| Country: Number of subjects enrolled | Brazil: 45 |
| Country: Number of subjects enrolled | Bulgaria: 16 |
| Country: Number of subjects enrolled | Canada: 1 |
| Country: Number of subjects enrolled | Chile: 16 |
| Country: Number of subjects enrolled | France: 3 |
| Country: Number of subjects enrolled | Germany: 24 |
| Country: Number of subjects enrolled | Hungary: 20 |
| Country: Number of subjects enrolled | India: 6 |
| Country: Number of subjects enrolled | Italy: 9 |
| Country: Number of subjects enrolled | Mexico: 34 |
| Country: Number of subjects enrolled | Peru: 34 |
| Country: Number of subjects enrolled | Philippines: 45 |
| Country: Number of subjects enrolled | Poland: 29 |
| Country: Number of subjects enrolled | Romania: 19 |

| | |
|---|---|
| Country: Number of subjects enrolled | South Africa: 20 |
| Country: Number of subjects enrolled | Spain: 28 |
| Country: Number of subjects enrolled | Thailand: 12 |
| Country: Number of subjects enrolled | United Kingdom: 13 |
| Country: Number of subjects enrolled | United States: 38 |
| Worldwide total number of subjects | 432 |
| EEA total number of subjects | 161 |

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) | 423 |
| From 65 to 84 years | 9 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 834 participants were screened out of which 402 participants did not meet eligibility criteria and were considered screen failures, and 432 participants were randomized into the study.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo |

Arm description:

Placebo matching to sifalimumab administered by intravenous infusion at a fixed dose of every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo matching to sifalimumab administered by intravenous infusion at a fixed dose of every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses.

| | |
|---|---|
| **Arm title** | Sifalimumab 200 milligram (mg) |

Arm description:

Sifalimumab 200 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Sifalimumab 200 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Sifalimumab 200 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses.

| | |
|---|---|
| **Arm title** | Sifalimumab 600 mg |

Arm description:

Sifalimumab 600 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Sifalimumab 600 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Sifalimumab 600 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses.

| **Arm title** | Sifalimumab 1,200 mg |
|---|---|

Arm description:

Sifalimumab 1,200 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Sifalimumab 1,200 mg |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Sifalimumab 1,200 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses.

| **Number of subjects in period 1** | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg |
|---|---|---|---|
| Started | 108 | 108 | 109 |
| Completed | 91 | 90 | 91 |
| Not completed | 17 | 18 | 18 |
| Adverse event, serious fatal | 2 | - | 2 |
| Consent withdrawn by subject | 8 | 8 | 6 |
| Pregnancy | - | 1 | 1 |
| Missed follow-up visit | - | 1 | 2 |
| Participant randomized in error | - | - | 1 |
| Early termination due to AE/SAE | 1 | 1 | - |
| Lost to follow-up | 5 | 2 | 3 |
| Lack of efficacy | 1 | 2 | 2 |
| Participant's refusal to continue | - | 3 | 1 |

| **Number of subjects in period 1** | Sifalimumab 1,200 mg |
|---|---|
| Started | 107 |
| Completed | 92 |
| Not completed | 15 |
| Adverse event, serious fatal | 2 |
| Consent withdrawn by subject | 8 |
| Pregnancy | - |

| | |
|---|---|
| Missed follow-up visit | 2 |
| Participant randomized in error | - |
| Early termination due to AE/SAE | - |
| Lost to follow-up | 1 |
| Lack of efficacy | 1 |
| Participant's refusal to continue | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo matching to sifalimumab administered by intravenous infusion at a fixed dose of every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses. | |
| Reporting group title | Sifalimumab 200 milligram (mg) |
| Reporting group description: | |
| Sifalimumab 200 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses. | |
| Reporting group title | Sifalimumab 600 mg |
| Reporting group description: | |
| Sifalimumab 600 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses. | |
| Reporting group title | Sifalimumab 1,200 mg |
| Reporting group description: | |
| Sifalimumab 1,200 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses. | |

| Reporting group values | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg |
|---|---|---|---|
| Number of subjects | 108 | 108 | 109 |
| Age categorical | | | |
| Units: Subjects | | | |
| Age Continuous \| | | | |
| Units: years | | | |
| arithmetic mean | 38.4 | 39.9 | 40.1 |
| standard deviation | ± 12.3 | ± 11.4 | ± 11.3 |
| Gender, Male/Female | | | |
| Units: participants | | | |
| Female | 101 | 103 | 98 |
| Male | 7 | 5 | 11 |

| Reporting group values | Sifalimumab 1,200 mg | Total | |
|---|---|---|---|
| Number of subjects | 107 | 432 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age Continuous \| | | | |
| Units: years | | | |
| arithmetic mean | 39.4 | | |
| standard deviation | ± 12.1 | - | |
| Gender, Male/Female | | | |
| Units: participants | | | |
| Female | 97 | 399 | |
| Male | 10 | 33 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo matching to sifalimumab administered by intravenous infusion at a fixed dose of every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses. | |
| Reporting group title | Sifalimumab 200 milligram (mg) |
| Reporting group description: | |
| Sifalimumab 200 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses. | |
| Reporting group title | Sifalimumab 600 mg |
| Reporting group description: | |
| Sifalimumab 600 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses. | |
| Reporting group title | Sifalimumab 1,200 mg |
| Reporting group description: | |
| Sifalimumab 1,200 mg administered by intravenous infusion every 2 weeks (14 days) for the first 3 doses (Days 1, 15, and 29) and then every 4 weeks (28 days) thereafter for 11 doses for a total of 14 doses. | |
| Subject analysis set title | Modified Intent-to-treat (mITT) Population |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| The mITT population included all randomized participants who received any investigational product and had a baseline primary efficacy measurement. | |
| Subject analysis set title | Safety Population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| The safety population included all participants who received any investigational product. | |

### Primary: Percentage of Participants Achieving a Response in Systemic Lupus Erythematosus Responder Index 4 (SRI [4])

| | |
|---|---|
| End point title | Percentage of Participants Achieving a Response in Systemic Lupus Erythematosus Responder Index 4 (SRI [4]) |
| End point description: | |
| SRI (4) responder is defined as: 1) a reduction in baseline Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) disease activity score of greater than or equal to (>=) 4 points (with increased deoxyribonucleic acid [DNA] binding item of SLEDAI-2K score based on the ANA Multi−Lyte® ANA−II Plus Test System); 2) no worsening in Physician Global Assessment (MDGA) (worsening is defined as an increase of >=0.3 from baseline on a 0-3 visual analogue scale) and 3) no worsening in British Isles Lupus Assessment Group (BILAG-2004) (worsening is defined as at least 1 new 'A' score or 2 new 'B' scores on the BILAG-2004 compared with baseline). The modified intent-to-treat (mITT) population included all randomized participants who received any investigational product and had a baseline primary efficacy measurement. | |
| End point type | Primary |
| End point timeframe: | |
| Day 365 | |

| End point values | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg | Sifalimumab 1,200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 108 | 108 | 108 | 107 |
| Units: percentage of participants | | | | |
| number (not applicable) | 45.4 | 58.3 | 56.5 | 59.8 |

**Statistical analyses**

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 200 milligram (mg) |
| Number of subjects included in analysis | 216 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.057 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.71 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.03 |
| upper limit | 2.71 |

| Statistical analysis title | Statistical analysis 2 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 600 mg |
| Number of subjects included in analysis | 216 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.094 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.6 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.01 |
| upper limit | 2.54 |

| Statistical analysis title | Statistical analysis 3 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 1,200 mg |

| | |
|---|---|
| Number of subjects included in analysis | 215 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.031 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.84 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.16 |
| upper limit | 2.94 |

## Primary: Percentage of Participants Achieving a Positive Response in SRI (4) in 4-Gene Interferon Test High Participants

| | |
|---|---|
| End point title | Percentage of Participants Achieving a Positive Response in SRI (4) in 4-Gene Interferon Test High Participants |

End point description:

SRI (4) responder is defined as: 1) a reduction in baseline SLEDAI-2K disease activity score of >=4 points (with increased DNA binding item of SLEDAI-2K score based on the ANA Multi−Lyte® ANA−II Plus Test System); 2) no worsening in Physician Global Assessment (MDGA) (worsening is defined as an increase of >=0.3 from baseline on a 0-3 visual analogue scale) and 3) no worsening in BILAG-2004 (worsening is defined as at least 1 new 'A' score or 2 new 'B' scores on the BILAG-2004 compared with baseline). The mITT population included all randomized participants who received any investigational product and had a baseline primary efficacy measurement.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Day 365

| **End point values** | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg | Sifalimumab 1,200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 88 | 87 | 88 | 87 |
| Units: percentage of participants | | | | |
| number (not applicable) | 42 | 57.5 | 50 | 57.5 |

## Statistical analyses

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 200 milligram (mg) |

| | |
|---|---|
| Number of subjects included in analysis | 175 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.042 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.88 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.13 |
| upper limit | 3.14 |

| **Statistical analysis title** | Statistical analysis 2 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 600 mg |
| Number of subjects included in analysis | 176 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.264 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.41 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 2.35 |

| **Statistical analysis title** | Statistical analysis 3 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 1,200 mg |
| Number of subjects included in analysis | 175 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.038 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.91 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.14 |
| upper limit | 3.19 |

## Secondary: Percentage of Participants on Greater Than or Equal to 10 mg/day Oral

## Prednisone (or Equivalent) at Baseline who Were Able to Reduce to Less Than or Equal to (<=) 7.5 mg/day

| End point title | Percentage of Participants on Greater Than or Equal to 10 mg/day Oral Prednisone (or Equivalent) at Baseline who Were Able to Reduce to Less Than or Equal to (<=) 7.5 mg/day |
|---|---|

End point description:

Percentage of participants on >=10 mg/day oral corticosteroids (OCS) at baseline who were able to taper it to <=7.5 mg/day by Day 365 were recorded. The mITT population included all randomized participants who received any investigational product and had a baseline primary efficacy measurement. Here, "N" signifies number of participants analyzed on >=10 mg/day oral prednisone (or equivalent) at baseline.

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

End point timeframe:

Day 365

| **End point values** | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg | Sifalimumab 1,200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 62 | 61 | 53 | 65 |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Reduce OCS to <=7.5 mg/day: Yes | 6.5 | 8.2 | 9.4 | 6.2 |
| Reduce OCS to <=7.5 mg/day: No | 93.5 | 91.8 | 90.6 | 93.8 |

### Statistical analyses

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 200 milligram (mg) |
| Number of subjects included in analysis | 123 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.808 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.19 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.37 |
| upper limit | 3.81 |

| **Statistical analysis title** | Statistical analysis 3 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 1,200 mg |

| | |
|---|---|
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.884 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.27 |
| upper limit | 3.02 |

| **Statistical analysis title** | Statistical analysis 2 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 600 mg |
| Number of subjects included in analysis | 115 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.598 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.45 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.45 |
| upper limit | 4.66 |

## Secondary: Percentage of Participants with a Cutaneous Lupus Erythematosus Disease Activity and Severity Index (CLASI) Activity Score Greater Than or Equal to (>=) 10 at Baseline Who Achieved a >= 4-point Reduction

| | |
|---|---|
| End point title | Percentage of Participants with a Cutaneous Lupus Erythematosus Disease Activity and Severity Index (CLASI) Activity Score Greater Than or Equal to (>=) 10 at Baseline Who Achieved a >= 4-point Reduction |

End point description:

The CLASI consists of two scores, the first summarizes the activity of the disease while the second is a measure of the damage done by the disease. Activity is scored on the basis of erythema, scale/hyperkeratosis, mucous membrane involvement, acute hair loss and non-scarring alopecia. Damage is scored in terms of dyspigmentation and scarring, including scarring alopecia. The percentage of participants with a CLASI activity score >=10 at baseline who achieved a clinically significant (>=4-point) reduction at Day 365 were reported. The mITT population included all randomized participants who received any investigational product and had a baseline primary efficacy measurement. Here, "N" signifies number of participants analyzed with a CLASI activity score >=10 at baseline.

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

End point timeframe:

Day 365

| **End point values** | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg | Sifalimumab 1,200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 35 | 33 | 33 | 26 |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Achieved >=4-point reduction: Yes | 48.6 | 72.7 | 57.6 | 73.1 |
| Achieved >=4-point reduction: No | 51.4 | 27.3 | 42.4 | 26.9 |

**Statistical analyses**

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 200 milligram (mg) |
| Number of subjects included in analysis | 68 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.044 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 2.92 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.22 |
| upper limit | 7.01 |

| **Statistical analysis title** | Statistical analysis 2 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 600 mg |
| Number of subjects included in analysis | 68 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.498 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.62 |
| upper limit | 3.19 |

| Statistical analysis title | Statistical analysis 3 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 1,200 mg |
| Number of subjects included in analysis | 61 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.049 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 3.03 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.2 |
| upper limit | 7.68 |

## Secondary: Percentage of Participants who Achieved a Greater Than 3-Point Improvement in the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale

| End point title | Percentage of Participants who Achieved a Greater Than 3-Point Improvement in the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue Scale |
|---|---|

End point description:

FACIT-F is a 13-item questionnaire. Participants scored each item on a 5-point scale: 0 (not at all) to 4 (very much). Larger the participant's response to the questions (with the exception of 2 negatively stated), greater was the participant's fatigue. For all questions, except for the 2 negatively stated ones, the code was reversed and a new score was calculated as (4 minus the participant's response). The sum of all responses resulted in the FACIT-Fatigue score for a total possible score of 0 (worse score) to 52 (better score). The mITT population included all randomized participants who received any investigational product and had a baseline primary efficacy measurement. Here, "N" signifies number of participants analyzed with a FACIT-fatigue score <49 at baseline.

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

End point timeframe:

Day 365

| End point values | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg | Sifalimumab 1,200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 105 | 105 | 102 | 101 |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Achieved > 3-point improvement: Yes | 30.5 | 38.1 | 42.2 | 35.6 |
| Achieved > 3-point improvement: No | 69.5 | 61.9 | 57.8 | 64.4 |

## Statistical analyses

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 200 milligram (mg) |
| Number of subjects included in analysis | 210 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.27 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.39 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 2.25 |

| **Statistical analysis title** | Statistical analysis 3 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 1,200 mg |
| Number of subjects included in analysis | 206 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.453 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.25 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 2.05 |

| **Statistical analysis title** | Statistical analysis 2 |
|---|---|
| Comparison groups | Placebo v Sifalimumab 600 mg |

| | |
|---|---|
| Number of subjects included in analysis | 207 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.077 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.69 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 1.04 |
| upper limit | 2.74 |

## Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (TESAEs)

| | |
|---|---|
| End point title | Number of Participants With Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (TESAEs) |

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent defined as events present at baseline that worsened in intensity after administration of investigational product or events absent at baseline that emerged after administration of investigational product, for the period extending until the end of participant participation in the study. The safety population included all participants who received any investigational product.

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

End point timeframe:

Day 1 up to Week 74

| End point values | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg | Sifalimumab 1,200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 108 | 108 | 108 | 107 |
| Units: participants | | | | |
| TEAE | 94 | 97 | 97 | 93 |
| TESAE | 19 | 16 | 22 | 21 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Abnormal Clinical Laboratory Parameters Reported as Treatment-Emergent Adverse Events (TEAEs)

| | |
|---|---|
| End point title | Number of Participants with Abnormal Clinical Laboratory |

| | |
|---|---|
| | Parameters Reported as Treatment-Emergent Adverse Events (TEAEs) |

End point description:

Laboratory investigations included hematology, serum chemistries and urinalysis parameters. Participants with clinically significant abnormalities in these laboratory investigations recorded as TEAEs were reported. The safety population included all participants who received any investigational product.

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

End point timeframe:

Day 1 up to Week 61

| **End point values** | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg | Sifalimumab 1,200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 108 | 108 | 108 | 107 |
| Units: participants | | | | |
| Anaemia | 1 | 4 | 4 | 2 |
| White blood cell count increased | 3 | 1 | 2 | 3 |
| Neutrophil count increased | 3 | 1 | 2 | 2 |
| Iron deficiency anaemia | 1 | 2 | 0 | 2 |
| Haemoglobin decreased | 0 | 1 | 0 | 1 |
| Lymphocyte count decreased | 2 | 1 | 1 | 0 |
| White blood cell count decreased | 1 | 0 | 1 | 1 |
| Autoimmune haemolytic anaemia | 1 | 1 | 0 | 0 |
| Eosinophilia | 0 | 0 | 0 | 1 |
| Haematocrit increased | 0 | 0 | 1 | 0 |
| Haemoglobin increased | 0 | 0 | 1 | 0 |
| Leukopenia | 0 | 1 | 0 | 0 |
| Lymphopenia | 1 | 1 | 0 | 0 |
| Neutropenia | 3 | 0 | 0 | 1 |
| Neutrophil count decreased | 1 | 0 | 0 | 1 |
| Platelet count increased | 0 | 0 | 1 | 0 |
| Red blood cell count decreased | 0 | 0 | 0 | 1 |
| Thrombocytopenia | 0 | 1 | 0 | 0 |
| Platelet count decreased | 2 | 0 | 0 | 0 |
| Monocyte count increased | 1 | 0 | 0 | 0 |
| Hypokalaemia | 4 | 1 | 4 | 5 |
| Alanine aminotransferase increased | 5 | 1 | 1 | 3 |
| Gamma-glutamyltransferase increased | 5 | 0 | 1 | 4 |
| Hypertriglyceridaemia | 2 | 1 | 1 | 3 |
| Dyslipidaemia | 2 | 0 | 2 | 2 |
| Hepatic enzyme increased | 2 | 2 | 2 | 0 |
| Aspartate aminotransferase increased | 2 | 1 | 0 | 2 |
| Blood creatine phosphokinase increased | 2 | 0 | 2 | 0 |
| Blood creatinine increased | 0 | 1 | 0 | 1 |
| Blood glucose increased | 1 | 0 | 0 | 2 |
| Hyperglycaemia | 1 | 0 | 0 | 2 |
| Transaminases increased | 1 | 0 | 1 | 1 |
| Blood potassium decreased | 0 | 1 | 1 | 0 |
| Low density lipoprotein increased | 0 | 1 | 1 | 0 |

| | | | | |
|---|---|---|---|---|
| Blood albumin decreased | 0 | 0 | 1 | 0 |
| Blood alkaline phosphatase decreased | 1 | 0 | 0 | 1 |
| Blood calcium increased | 1 | 0 | 1 | 0 |
| Blood cholesterol increased | 0 | 0 | 1 | 0 |
| Blood homocysteine increased | 0 | 0 | 1 | 0 |
| Liver function test abnormal | 1 | 0 | 1 | 0 |
| Hyperlipidaemia | 0 | 0 | 0 | 1 |
| Hypoalbuminaemia | 2 | 0 | 1 | 0 |
| Hypoglycaemia | 0 | 0 | 0 | 1 |
| Blood bilirubin increased | 1 | 0 | 0 | 0 |
| Hypocalcaemia | 1 | 0 | 0 | 0 |
| Blood triglycerides increased | 1 | 0 | 1 | 0 |
| Hyperbilirubinaemia | 0 | 0 | 1 | 0 |
| Hypertransaminasaemia | 0 | 0 | 1 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Abnormal Vital Signs Reported as Treatment-Emergent Adverse Events (TEAEs)

| End point title | Number of Participants With Abnormal Vital Signs Reported as Treatment-Emergent Adverse Events (TEAEs) |
|---|---|

End point description:

Vital sign assessments included blood pressure, pulse rate, temperature, weight and respiratory rate. Vital signs abnormalities recorded as TEAEs were reported. The safety population included all participants who received any investigational product.

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

End point timeframe:

Day 1 up to Week 61

| End point values | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg | Sifalimumab 1,200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 108 | 108 | 108 | 107 |
| Units: participants | | | | |
| Pyrexia | 3 | 2 | 6 | 7 |
| Hypertension | 7 | 4 | 5 | 4 |
| Weight increased | 0 | 1 | 2 | 2 |
| Blood pressure increased | 1 | 2 | 1 | 0 |
| Chills | 1 | 2 | 0 | 1 |
| Hypertensive crisis | 0 | 0 | 0 | 1 |
| Orthostatic hypotension | 1 | 0 | 0 | 1 |
| Weight decreased | 1 | 0 | 0 | 1 |
| Hypotension | 1 | 0 | 0 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Abnormal Electrocardiogram (ECG) Findings Reported as TEAEs

| End point title | Number of Participants With Abnormal Electrocardiogram (ECG) Findings Reported as TEAEs |
|---|---|

End point description:

The 12-lead ECG data were summarized and evaluated. Number of participants with clinically significant abnormal ECG findings as assessed by cardiologist were recorded and reported as TEAEs. The safety population included all participants who received any investigational product.

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

End point timeframe:

Day 1 up to Week 56

| End point values | Placebo | Sifalimumab 200 milligram (mg) | Sifalimumab 600 mg | Sifalimumab 1,200 mg |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 108 | 108 | 108 | 107 |
| Units: participants | 2 | 0 | 1 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Day 1 up to Week 74 | |
| Adverse event reporting additional description: | |
| TEAE defined as events present at baseline that worsened in intensity after administration of investigational product or events absent at baseline that emerged after administration of investigational product, for the period extending until the end of participant participation in the study. | |
| Assessment type | Non-systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 17.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Sifalimumab 200 milligram (mg) |
| Reporting group description: | |
| Sifalimumab 200 milligram (mg) administered intravenously for 48 weeks (Day 337). | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Placebo matching to sifalimumab administered intravenously for 48 weeks (Day 337). | |
| Reporting group title | Sifalimumab 1,200 mg |
| Reporting group description: | |
| Sifalimumab 1,200 mg administered intravenously for 48 weeks (Day 337). | |
| Reporting group title | Sifalimumab 600 mg |
| Reporting group description: | |
| Sifalimumab 600 mg administered intravenously for 48 weeks (Day 337). | |

| Serious adverse events | Sifalimumab 200 milligram (mg) | Placebo | Sifalimumab 1,200 mg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 108 (14.81%) | 19 / 108 (17.59%) | 21 / 107 (19.63%) |
| number of deaths (all causes) | 0 | 2 | 2 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung neoplasm malignant | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| 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 | | | |
| Hypertension | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic limb pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Peripheral artery thrombosis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Peripheral embolism | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Abortion spontaneous incomplete | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ectopic pregnancy | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Cervical dysplasia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| 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 | | | |
| Asthma | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Laryngeal polyp | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 embolism | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 hypertension | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 | | | |
| Fall | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Fracture | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Head injury | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Infusion related reaction | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Meniscus injury | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Muscle rupture | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Spinal compression fracture | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Stab wound | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| **Cardiac disorders** | | | |
| Acute myocardial infarction | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Angina pectoris | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 arrest | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cardio-respiratory arrest | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 | | | |
| Ischaemic stroke | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Simple partial seizures | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Syncope | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Transient ischaemic attack | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vasculitis cerebral | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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** | | | |
| Anaemia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 2 / 107 (1.87%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Gastrointestinal disorders** | | | |
| Ascites | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Diverticulum oesophageal | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Gastritis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis haemorrhagic | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Intussusception | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Irritable bowel syndrome | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Lip ulceration | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salivary gland calculus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Small intestinal perforation | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Tongue oedema | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 | | | |
| Skin ulcer | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 | | | |
| Renal failure acute | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Flank pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Foot deformity | | | |

| | | | |
|---|---|---|---|
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Systemic lupus erythematosus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 108 (3.70%) | 3 / 108 (2.78%) | 3 / 107 (2.80%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 1 / 108 (0.93%) | 0 / 107 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 1 / 108 (0.93%) | 0 / 107 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Corneal infection | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Encephalitis viral | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Enterocolitis bacterial | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Epiglottitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Erysipelas | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Gastroenteritis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Infectious colitis<br>alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| 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<br>alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Lobar pneumonia<br>alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection<br>alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ludwig angina<br>alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Meningitis bacterial<br>alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ophthalmic herpes zoster<br>alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parotitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Pneumonia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 1 / 108 (0.93%) | 2 / 107 (1.87%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Progressive multifocal leukoencephalopathy | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |
| Pyelonephritis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Pyelonephritis acute | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 108 (1.85%) | 1 / 108 (0.93%) | 0 / 107 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic embolus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 |
| Septic shock | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 2 / 108 (1.85%) | 0 / 107 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| Soft tissue infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 0 / 108 (0.00%) | 0 / 107 (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 respiratory tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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 |

| | | | |
|---|---|---|---|
| Urinary tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 1 / 108 (0.93%) | 0 / 107 (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** | Sifalimumab 600 mg | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 22 / 108 (20.37%) | | |
| number of deaths (all causes) | 2 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung neoplasm malignant | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ischaemic limb pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral artery thrombosis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral embolism | | | |
| alternative assessment type: | | | |

| | | | |
|---|---|---|---|
| Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abortion spontaneous incomplete | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ectopic pregnancy | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Cervical dysplasia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | | |
|---|---|---|---|---|
| Asthma | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Epistaxis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Laryngeal polyp | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary embolism | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary hypertension | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Injury, poisoning and procedural complications | | | | |
| Fall | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fracture | | | | |
| alternative assessment type: Systematic | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Head injury | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Humerus fracture | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infusion related reaction | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Meniscus injury | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscle rupture | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal compression fracture | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|---|---|---|---|---|
| Stab wound | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac disorders | | | | |
| Acute myocardial infarction | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Angina pectoris | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac arrest | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardio-respiratory arrest | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Mitral valve incompetence | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Nervous system disorders | | | | |
| Ischaemic stroke | | | | |
| alternative assessment type: Systematic | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Simple partial seizures | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Syncope | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Transient ischaemic attack | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vasculitis cerebral | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood and lymphatic system disorders | | | | |
| Anaemia | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neutropenia | | | | |
| alternative assessment type: Systematic | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Ascites | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diverticulum oesophageal | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis haemorrhagic | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intussusception | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Irritable bowel syndrome | | | |
| alternative assessment type: Systematic | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lip ulceration | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Salivary gland calculus | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Small intestinal perforation | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tongue oedema | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin and subcutaneous tissue disorders | | | | |
| Skin ulcer | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal and urinary disorders | | | | |
| Renal failure acute | | | | |
| alternative assessment type: Systematic | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Flank pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Foot deformity | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteonecrosis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Systemic lupus erythematosus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 7 / 108 (6.48%) | | |
| occurrences causally related to treatment / all | 1 / 9 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| alternative assessment type: Systematic | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchitis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Corneal infection | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Encephalitis viral | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis bacterial | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Epiglottitis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|---|---|---|---|---|
| Erysipelas | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infectious colitis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lobar pneumonia | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection | | | | |
| alternative assessment type: Systematic | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ludwig angina | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningitis bacterial | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ophthalmic herpes zoster | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Parotitis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonitis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|---|---|---|---|---|
| Progressive multifocal leukoencephalopathy | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyelonephritis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyelonephritis acute | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory tract infection | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Septic embolus | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Septic shock | | | | |
| alternative assessment type: Systematic | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Soft tissue infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 2 %

| **Non-serious adverse events** | Sifalimumab 200 milligram (mg) | Placebo | Sifalimumab 1,200 mg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 97 / 108 (89.81%) | 94 / 108 (87.04%) | 93 / 107 (86.92%) |
| Vascular disorders | | | |
| Hypertension | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 108 (3.70%) | 7 / 108 (6.48%) | 3 / 107 (2.80%) |
| occurrences (all) | 4 | 8 | 3 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 108 (1.85%) | 3 / 108 (2.78%) | 7 / 107 (6.54%) |
| occurrences (all) | 3 | 4 | 10 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 7 / 108 (6.48%) | 7 / 108 (6.48%) | 6 / 107 (5.61%) |
| occurrences (all) | 7 | 7 | 6 |
| Epistaxis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 108 (3.70%) | 1 / 108 (0.93%) | 2 / 107 (1.87%) |
| occurrences (all) | 4 | 1 | 2 |
| Oropharyngeal pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 108 (3.70%) | 4 / 108 (3.70%) | 0 / 107 (0.00%) |
| occurrences (all) | 4 | 5 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 6 / 108 (5.56%) | 3 / 108 (2.78%) | 7 / 107 (6.54%) |
| occurrences (all) | 6 | 3 | 8 |
| Insomnia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 7 / 108 (6.48%) | 4 / 108 (3.70%) | 1 / 107 (0.93%) |
| occurrences (all) | 8 | 4 | 1 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 5 / 108 (4.63%) | 3 / 107 (2.80%) |
| occurrences (all) | 1 | 7 | 5 |
| Gamma-glutamyltransferase increased | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 5 / 108 (4.63%) | 4 / 107 (3.74%) |
| occurrences (all) | 0 | 7 | 5 |
| White blood cell count increased | | | |
| alternative assessment type: | | | |

| | | | |
|---|---|---|---|
| Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 3 / 108 (2.78%) | 3 / 107 (2.80%) |
| occurrences (all) | 1 | 4 | 5 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | 3 / 108 (2.78%) | 1 / 107 (0.93%) |
| occurrences (all) | 2 | 4 | 1 |
| Infusion related reaction | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 8 / 108 (7.41%) | 5 / 108 (4.63%) | 5 / 107 (4.67%) |
| occurrences (all) | 17 | 10 | 10 |
| Nervous system disorders | | | |
| Dizziness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 108 (4.63%) | 5 / 108 (4.63%) | 5 / 107 (4.67%) |
| occurrences (all) | 6 | 5 | 5 |
| Headache | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 16 / 108 (14.81%) | 15 / 108 (13.89%) | 12 / 107 (11.21%) |
| occurrences (all) | 18 | 24 | 13 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | 1 / 108 (0.93%) | 1 / 107 (0.93%) |
| occurrences (all) | 3 | 1 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 108 (0.00%) | 2 / 108 (1.85%) | 4 / 107 (3.74%) |
| occurrences (all) | 0 | 2 | 4 |
| Abdominal pain upper | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 4 / 108 (3.70%) | 4 / 107 (3.74%) |
| occurrences (all) | 1 | 5 | 4 |

| | | | |
|---|---|---|---|
| Constipation | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 2 / 108 (1.85%) | 5 / 107 (4.67%) |
| occurrences (all) | 1 | 2 | 5 |
| Diarrhoea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 7 / 108 (6.48%) | 8 / 108 (7.41%) | 5 / 107 (4.67%) |
| occurrences (all) | 7 | 9 | 5 |
| Dyspepsia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | 3 / 108 (2.78%) | 4 / 107 (3.74%) |
| occurrences (all) | 3 | 3 | 4 |
| Gastritis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | 0 / 108 (0.00%) | 3 / 107 (2.80%) |
| occurrences (all) | 3 | 0 | 3 |
| Nausea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 108 (3.70%) | 8 / 108 (7.41%) | 5 / 107 (4.67%) |
| occurrences (all) | 5 | 12 | 7 |
| Vomiting | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 5 / 108 (4.63%) | 3 / 107 (2.80%) |
| occurrences (all) | 1 | 5 | 3 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 7 / 108 (6.48%) | 2 / 108 (1.85%) | 5 / 107 (4.67%) |
| occurrences (all) | 8 | 2 | 8 |
| Rash | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 1 / 108 (0.93%) | 6 / 107 (5.61%) |
| occurrences (all) | 1 | 1 | 6 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Arthralgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | 3 / 108 (2.78%) | 5 / 107 (4.67%) |
| occurrences (all) | 3 | 6 | 5 |
| Back pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | 3 / 108 (2.78%) | 5 / 107 (4.67%) |
| occurrences (all) | 3 | 3 | 5 |
| Systemic lupus erythematosus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 34 / 108 (31.48%) | 35 / 108 (32.41%) | 26 / 107 (24.30%) |
| occurrences (all) | 42 | 56 | 46 |
| Infections and infestations | | | |
| Bronchitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 11 / 108 (10.19%) | 8 / 108 (7.41%) | 15 / 107 (14.02%) |
| occurrences (all) | 15 | 8 | 20 |
| Conjunctivitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 108 (3.70%) | 4 / 108 (3.70%) | 2 / 107 (1.87%) |
| occurrences (all) | 5 | 5 | 2 |
| Gastroenteritis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 108 (4.63%) | 5 / 108 (4.63%) | 4 / 107 (3.74%) |
| occurrences (all) | 6 | 6 | 4 |
| Herpes zoster | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 108 (4.63%) | 1 / 108 (0.93%) | 8 / 107 (7.48%) |
| occurrences (all) | 6 | 1 | 8 |
| Influenza | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | 4 / 108 (3.70%) | 5 / 107 (4.67%) |
| occurrences (all) | 3 | 4 | 5 |
| Nasopharyngitis | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 12 / 108 (11.11%) | 10 / 108 (9.26%) | 9 / 107 (8.41%) |
| occurrences (all) | 14 | 17 | 12 |
| Oral herpes | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | 5 / 108 (4.63%) | 4 / 107 (3.74%) |
| occurrences (all) | 7 | 6 | 5 |
| Pharyngitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | 4 / 108 (3.70%) | 12 / 107 (11.21%) |
| occurrences (all) | 3 | 5 | 12 |
| Respiratory tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | 3 / 108 (2.78%) | 3 / 107 (2.80%) |
| occurrences (all) | 1 | 5 | 4 |
| Sinusitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | 3 / 108 (2.78%) | 5 / 107 (4.67%) |
| occurrences (all) | 2 | 3 | 7 |
| Upper respiratory tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 10 / 108 (9.26%) | 9 / 108 (8.33%) | 15 / 107 (14.02%) |
| occurrences (all) | 16 | 12 | 23 |
| Urinary tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 22 / 108 (20.37%) | 14 / 108 (12.96%) | 18 / 107 (16.82%) |
| occurrences (all) | 25 | 19 | 25 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | 2 / 108 (1.85%) | 2 / 107 (1.87%) |
| occurrences (all) | 2 | 2 | 2 |
| Hypokalaemia | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 108 (0.93%) | 4 / 108 (3.70%) | 5 / 107 (4.67%) |
| occurrences (all) | 1 | 5 | 7 |

| **Non-serious adverse events** | Sifalimumab 600 mg | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 97 / 108 (89.81%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 108 (4.63%) | | |
| occurrences (all) | 5 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 6 / 108 (5.56%) | | |
| occurrences (all) | 10 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 108 (4.63%) | | |
| occurrences (all) | 5 | | |
| Epistaxis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | | |
| occurrences (all) | 3 | | |
| Oropharyngeal pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | | |
| occurrences (all) | 2 | | |
| Insomnia | | | |
| alternative assessment type: | | | |

| | | | |
|---|---|---|---|
| Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | | |
| occurrences (all) | 3 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences (all) | 1 | | |
| Gamma-glutamyltransferase increased | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences (all) | 2 | | |
| White blood cell count increased | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | | |
| occurrences (all) | 4 | | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | | |
| occurrences (all) | 3 | | |
| Infusion related reaction | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 7 / 108 (6.48%) | | |
| occurrences (all) | 9 | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | | |
| occurrences (all) | 2 | | |
| Headache | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 15 / 108 (13.89%) | | |
| occurrences (all) | 37 | | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Anaemia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 108 (3.70%) | | |
| occurrences (all) | 4 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 6 / 108 (5.56%) | | |
| occurrences (all) | 7 | | |
| Abdominal pain upper | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 5 / 108 (4.63%) | | |
| occurrences (all) | 5 | | |
| Constipation | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | | |
| occurrences (all) | 2 | | |
| Diarrhoea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 9 / 108 (8.33%) | | |
| occurrences (all) | 9 | | |
| Dyspepsia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences (all) | 1 | | |
| Gastritis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | | |
| occurrences (all) | 5 | | |
| Nausea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 7 / 108 (6.48%) | | |
| occurrences (all) | 11 | | |
| Vomiting | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 6 / 108 (5.56%) | | |
| occurrences (all) | 8 | | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | | |
| occurrences (all) | 3 | | |
| Rash | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 108 (1.85%) | | |
| occurrences (all) | 2 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 9 / 108 (8.33%) | | |
| occurrences (all) | 11 | | |
| Back pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 8 / 108 (7.41%) | | |
| occurrences (all) | 8 | | |
| Systemic lupus erythematosus | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 31 / 108 (28.70%) | | |
| occurrences (all) | 46 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 108 (3.70%) | | |
| occurrences (all) | 7 | | |
| Conjunctivitis | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis | | | |
| alternative assessment type: Systematic | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 5 / 108 (4.63%) | | | |
| occurrences (all) | 6 | | | |
| Herpes zoster | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 4 / 108 (3.70%) | | | |
| occurrences (all) | 4 | | | |
| Influenza | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 1 / 108 (0.93%) | | | |
| occurrences (all) | 1 | | | |
| Nasopharyngitis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 13 / 108 (12.04%) | | | |
| occurrences (all) | 15 | | | |
| Oral herpes | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | | | |
| occurrences (all) | 4 | | | |
| Pharyngitis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 6 / 108 (5.56%) | | | |
| occurrences (all) | 9 | | | |
| Respiratory tract infection | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 3 / 108 (2.78%) | | | |
| occurrences (all) | 3 | | | |
| Sinusitis | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 4 / 108 (3.70%) | | | |
| occurrences (all) | 4 | | | |
| Upper respiratory tract infection | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 17 / 108 (15.74%) | | | |
| occurrences (all) | 27 | | | |

| | | | |
|---|---|---|---|
| Urinary tract infection<br>alternative assessment type: Systematic<br>subjects affected / exposed<br>occurrences (all) | 17 / 108 (15.74%)<br>22 | | |
| Metabolism and nutrition disorders<br>Diabetes mellitus<br>alternative assessment type: Systematic<br>subjects affected / exposed<br>occurrences (all) | 3 / 108 (2.78%)<br>4 | | |
| Hypokalaemia<br>alternative assessment type: Systematic<br>subjects affected / exposed<br>occurrences (all) | 4 / 108 (3.70%)<br>5 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 06 June 2011 | The overall reason for the amendment was to include the following changes: Changes in eligibility criteria. Added instruction for participants who entered the study with indeterminate QuantiFERON-TB Gold blood test results. Changes in the hepatitis B virus deoxyribonucleic acid (HBV DNA) level required to qualify and remain in the study from "<=300 copies/mL" to "HBV DNA detected by reflex testing by the central lab at screening or at any time for the duration of the study." Also specified that the frequency of HBV DNA testing in isolated Hepatitis B core positive participants was to be done. Text to clarify that body temperature should be taken orally, removed text regarding the collection of serum samples for the assessment of safety biomarkers during infusion, hypersensitivity, and anaphylactic reactions and text to clarify corticosteroid tapering due to decreased SLE activity after Day 85. Changes in flow cytometry sample collection due to extension of the follow-up period from 90 to 180 days. An additional Clinical Evaluation Questionnaire (CEQ) assessment was to be performed. Amended to include only 200 participants would participate in sample collection for acute phase reactants/biomarkers, all flow cytometry data would remain blinded until the end of the study, and only plasma samples were to be collected for optional biomarker repository samples. To characterize proteomic sample collection, to characterize IFN bioassay sample collection, to reflect the new estimated volume of blood that was to be collected. To clarify that skin photographs would not be obtained from participants who did not present with active skin disease at screening or day 1, to define and describe the method of collection for Adverse Events of Interest (AESIs), sulfasalazine to the list of restricted medications. |
| 28 August 2012 | The overall reason for the amendment was to include the following changes: Change in description of sifalimumab dosing, text to reduce overall sample size from 544 participants to 400 participants based on a 20 percent (%) improvement of sifalimumab over placebo in the SRI. Participants were in screening at the time of the 400th subject was randomized, if eligible participants would have been allowed to be randomized into the study. Change in serum sample collection time points. The number of diagnostic test-positive participants per treatment group was revised to 60 participants and the minimum detectable difference was also revised. |
| 23 January 2013 | The overall reason for the amendment was to include the following changes: To describe an unblinded interim analysis was planned for the study, which was performed by a limited number of sponsor personnel. To describe the collection of optional urine biomarker samples from eligible participants. To describe that Farr assay testing was to be performed on Day 169. Sample size of diagnostic test-positive participants per treatment group was increased from 60 to 80. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported