



Clinical trial results:

A Phase 3, randomized, double-blind, placebo-controlled, multicenter study of the efficacy and safety of four 12-week treatment cycles (48 weeks total) of epratuzumab in systemic lupus erythematosus subjects with moderate to severe disease (EMBODY 1)

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2010-018563-41 |
| Trial protocol | BE ES DE CZ GB BG LT EE IT |
| Global end of trial date | 15 May 2015 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 06 December 2020 |
| First version publication date | 29 May 2016 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Alignment with final posting on ClinicalTrials.gov after NIH review. |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | SL0009 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01262365 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | UCB, Inc. |
| Sponsor organisation address | 1950 Lake Park Drive, Smyrna, United States, GA 30080 |
| Public contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com |
| Scientific contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.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 | 24 June 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 May 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To confirm the clinical efficacy of epratuzumab in the treatment of subjects with moderate to severe general Systemic Lupus Erythematosus (SLE) despite standard of care treatments (i.e., corticosteroids, and potentially antimalarials and immunosuppressants) continued from Baseline.

Protection of trial subjects:

Patients were pre-medicated prior to infusion of investigational medicinal product (IMP) to prevent infusion reactions. During the conduct of the study all subjects were closely monitored.

Background therapy:

- Subjects must be receiving concomitant oral corticosteroids within the range of 5 to 60 mg/day prednisone equivalents, dependent on the investigator's assessment of disease activity, at a stable dose for at least 5 days (± 1 day) prior to Week 0 (Visit 2) and the first study drug infusion. Tapering of oral corticosteroids after Week 4 (Visit 6) to a target dose of ≤ 7.5 mg/day prednisone equivalents is encouraged during the study.
- If the subject is receiving concomitant antimalarials, they must have been receiving them for at least 12 weeks prior to Screening/Baseline (Visit 1), with a stable dose regimen for at least 28 days (± 1 day) prior to Week 0 (Visit 2) and the first study drug infusion. The antimalarial dose should be continued at a stable dose (same as Baseline dose) during the study.
- If the subject is receiving concomitant immunosuppressants, they must be on a stable dose for at least 28 days (± 1 day) prior to Week 0 (Visit 2) and the first study drug infusion. The immunosuppressants dose should be continued at a stable dose (same as Baseline dose) during the study.
- Subjects receiving memantine, bromocriptine (Parlodel), danazol, dapsons, dehydroepiandrosterone, or retinoids must be on a stable dose for 28 days (± 1 day) prior to Visit 2 and the first study drug infusion. The dose must remain stable during the study until Week 24 (Visit 14), after which time it may be held stable or decreased based on the investigator's judgment of the subject's disease activity and health status.

Evidence for comparator:

Not applicable

| | |
|---|------------------|
| Actual start date of recruitment | 09 December 2010 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 4 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Australia: 43 |
| Country: Number of subjects enrolled | Belgium: 25 |
| Country: Number of subjects enrolled | Brazil: 50 |
| Country: Number of subjects enrolled | Bulgaria: 59 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Czechia: 30 |
| Country: Number of subjects enrolled | Estonia: 4 |
| Country: Number of subjects enrolled | France: 22 |
| Country: Number of subjects enrolled | Germany: 22 |
| Country: Number of subjects enrolled | India: 9 |
| Country: Number of subjects enrolled | Israel: 38 |
| Country: Number of subjects enrolled | Italy: 14 |
| Country: Number of subjects enrolled | Lithuania: 24 |
| Country: Number of subjects enrolled | Mexico: 15 |
| Country: Number of subjects enrolled | Romania: 39 |
| Country: Number of subjects enrolled | Russian Federation: 11 |
| Country: Number of subjects enrolled | Korea, Republic of: 14 |
| Country: Number of subjects enrolled | Spain: 37 |
| Country: Number of subjects enrolled | Taiwan: 33 |
| Country: Number of subjects enrolled | United Kingdom: 11 |
| Country: Number of subjects enrolled | United States: 293 |
| Worldwide total number of subjects | 793 |
| EEA total number of subjects | 287 |

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) | 770 |
| From 65 to 84 years | 23 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study started to enroll patients in December 2010 and concluded in May 2015.

Pre-assignment

Screening details:

Participant Flow refers to the Randomized Set (RS).

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 | Assessor, Investigator, Subject, Carer |

Arms

| | |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo (RS) |

Arm description:

Placebo infusions delivered weekly for a total of 4 weeks over four 12-week treatment cycles

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

Dosage and administration details:

weekly

| | |
|------------------|---|
| Arm title | Epratuzumab 1200 mg every other week (RS) |
|------------------|---|

Arm description:

1200 mg infusions delivered every other week for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles and placebo infusions delivered every other week for a total of 4 weeks over four 12-week treatment cycles

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Epratuzumab |
| Investigational medicinal product code | Emab |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

600 mg every week, 1200 mg every other week

| | |
|------------------|----------------------------------|
| Arm title | Epratuzumab 600 mg per week (RS) |
|------------------|----------------------------------|

Arm description:

600 mg infusions delivered weekly for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles

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

| | |
|--|-----------------------|
| Investigational medicinal product name | Epratuzumab |
| Investigational medicinal product code | Emab |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

600 mg every week, 1200 mg every other week

| Number of subjects in period 1 | Placebo (RS) | Epratuzumab 1200 mg every other week (RS) | Epratuzumab 600 mg per week (RS) |
|--------------------------------|--------------|---|----------------------------------|
| | | | |
| Started | 266 | 262 | 265 |
| Completed | 176 | 181 | 171 |
| Not completed | 90 | 81 | 94 |
| Adverse event, serious fatal | 1 | 2 | 1 |
| sponsor decision | 1 | 1 | - |
| Randomization error | 1 | - | 2 |
| Toxicity related to study drug | - | 1 | - |
| Patient pregnant | 1 | - | 1 |
| Patient unavailable | - | - | 1 |
| Consent withdrawn by subject | 17 | 22 | 22 |
| Suspected pregnancy | 1 | - | - |
| Adverse event, non-fatal | 26 | 16 | 11 |
| Cannot tolerate the protocol | - | 1 | - |
| Non-compliance | 1 | - | 2 |
| Lost to follow-up | 3 | 7 | 6 |
| Lack of efficacy | 35 | 30 | 47 |
| Protocol deviation | 3 | 1 | 1 |

Baseline characteristics

Subject analysis sets

| | |
|--|--|
| Subject analysis set title | Placebo (Weekly infusion) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Placebo infusions delivered weekly for a total of 4 weeks over four 12-week treatment cycles | |
| Subject analysis set title | Epratuzumab 1200 mg every other week |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: 1200 mg infusions delivered every other week for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles and placebo infusions delivered every other week for a total of 4 weeks over four 12-week treatment cycles | |
| Subject analysis set title | Epratuzumab 600 mg per week |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: 600 mg infusions delivered weekly for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles | |
| Subject analysis set title | Placebo (Weekly infusion) FAS |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Placebo infusions delivered weekly for a total of 4 weeks over four 12-week treatment cycles | |
| Subject analysis set title | Epratuzumab 1200 mg every other week (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: 1200 mg infusions delivered every other week for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles and placebo infusions delivered every other week for a total of 4 weeks over four 12-week treatment cycles | |
| Subject analysis set title | Epratuzumab 600 mg per week (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: 600 mg infusions delivered weekly for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles | |

| Reporting group values | Placebo (Weekly infusion) | Epratuzumab 1200 mg every other week | Epratuzumab 600 mg per week |
|---------------------------------------|---------------------------|--------------------------------------|-----------------------------|
| Number of subjects | 263 | 259 | 264 |
| Age categorical Units: Subjects | | | |
| ≤18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 252 | 254 | 257 |
| ≥65 years | 11 | 5 | 7 |
| Age continuous Units: years | | | |
| arithmetic mean | 41.4 | 42.5 | 42.3 |
| standard deviation | ± 12.6 | ± 11.8 | ± 11.4 |
| Gender categorical Units: Subjects | | | |
| Female | 250 | 243 | 242 |
| Male | 13 | 16 | 22 |

| Reporting group values | Placebo (Weekly infusion) FAS | Epratuzumab 1200 mg every other week (FAS) | Epratuzumab 600 mg per week (FAS) |
|---------------------------------------|-------------------------------|--|-----------------------------------|
| Number of subjects | 249 | 244 | 248 |
| Age categorical Units: Subjects | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 238 | 241 | 241 |
| >=65 years | 11 | 3 | 7 |
| Age continuous Units: years | | | |
| arithmetic mean | 41.2 | 42.2 | 42.2 |
| standard deviation | ± 12.8 | ± 11.7 | ± 11.4 |
| Gender categorical Units: Subjects | | | |
| Female | 237 | 228 | 226 |
| Male | 12 | 16 | 22 |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Placebo (RS) |
| Reporting group description: Placebo infusions delivered weekly for a total of 4 weeks over four 12-week treatment cycles | |
| Reporting group title | Epratuzumab 1200 mg every other week (RS) |
| Reporting group description: 1200 mg infusions delivered every other week for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles and placebo infusions delivered every other week for a total of 4 weeks over four 12-week treatment cycles | |
| Reporting group title | Epratuzumab 600 mg per week (RS) |
| Reporting group description: 600 mg infusions delivered weekly for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles | |
| Subject analysis set title | Placebo (Weekly infusion) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Placebo infusions delivered weekly for a total of 4 weeks over four 12-week treatment cycles | |
| Subject analysis set title | Epratuzumab 1200 mg every other week |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: 1200 mg infusions delivered every other week for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles and placebo infusions delivered every other week for a total of 4 weeks over four 12-week treatment cycles | |
| Subject analysis set title | Epratuzumab 600 mg per week |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: 600 mg infusions delivered weekly for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles | |
| Subject analysis set title | Placebo (Weekly infusion) FAS |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Placebo infusions delivered weekly for a total of 4 weeks over four 12-week treatment cycles | |
| Subject analysis set title | Epratuzumab 1200 mg every other week (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: 1200 mg infusions delivered every other week for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles and placebo infusions delivered every other week for a total of 4 weeks over four 12-week treatment cycles | |
| Subject analysis set title | Epratuzumab 600 mg per week (FAS) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: 600 mg infusions delivered weekly for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles | |

Primary: The percent of subjects meeting treatment response criteria at Week 48 according to a combined response index

| | |
|--|---|
| End point title | The percent of subjects meeting treatment response criteria at Week 48 according to a combined response index |
| End point description: Percentages are based on the number of subjects in the relevant treatment group within the Full Analysis Set. The combined response index incorporated criteria for achievement of responder status from the: British Isles Lupus Assessment Group Index (BILAG-2004)- improvement from study entry or | |

no worsening in other organ systems, Systemic Lupus Erythematosus Disease Activity Index (SLEDAI; Version 2000, also known as SLEDAI-2K) - no worsening compared to study entry, physician's global assessment of disease activity(PGA)- no worsening compared to study entry, and concomitant medications- no changes.

The Full Analysis Set (FAS) consisted of all subjects in the Randomized Set (RS) who had received at least 1 partial dose of study drug, with the exception of 45 subjects who were randomized at site 071, located in the USA, who were excluded from the FAS.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| At Week 48 | |

| End point values | Placebo (Weekly infusion) FAS | Epratuzumab 1200 mg every other week (FAS) | Epratuzumab 600 mg per week (FAS) | |
|-----------------------------------|-------------------------------------|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 249 | 244 | 248 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Responder | 34.1 | 39.8 | 37.5 | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical Analysis 1 |
| Statistical analysis description: | |
| Odds Ratio: Epratuzumab/Placebo calculated using logistic regression with factors for treatment, region, and baseline disease status. | |
| Comparison groups | Placebo (Weekly infusion) FAS v Epratuzumab 1200 mg every other week (FAS) |
| Number of subjects included in analysis | 493 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.175 ^[1] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.307 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.888 |
| upper limit | 1.923 |

Notes:

[1] - p-values have been calculated using logistic regression with factors for treatment, region, and baseline disease status.

| | |
|---|---|
| Statistical analysis title | Statistical Analysis 2 |
| Statistical analysis description: | |
| Odds Ratio: Epratuzumab/Placebo calculated using logistic regression with factors for treatment, region, and baseline disease status. | |
| Comparison groups | Placebo (Weekly infusion) FAS v Epratuzumab 600 mg per week (FAS) |

| | |
|---|------------------------|
| Number of subjects included in analysis | 497 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.442 ^[2] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.164 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.79 |
| upper limit | 1.714 |

Notes:

[2] - p-values have been calculated using logistic regression with factors for treatment, region, and baseline disease status.

Secondary: The percent of subjects meeting treatment response criteria at Week 24 according to a combined response index

| | |
|-----------------|---|
| End point title | The percent of subjects meeting treatment response criteria at Week 24 according to a combined response index |
|-----------------|---|

End point description:

Percentages are based on the number of subjects in the relevant treatment group within the Full Analysis Set. The combined response index incorporated criteria for achievement of responder status from the: British Isles Lupus Assessment Group Index (BILAG-2004)- improvement from study entry or no worsening in other organ systems, Systemic Lupus Erythematosus Disease Activity Index (SLEDAI; Version 2000, also known as SLEDAI-2K) - no worsening compared to study entry, physician's global assessment of disease activity(PGA)- no worsening compared to study entry, and concomitant medications- no changes.

The Full Analysis Set (FAS) consisted of all subjects in the Randomized Set (RS) who had received at least 1 partial dose of study drug, with the exception of 45 subjects who were randomized at site 071, located in the USA, who were excluded from the FAS.

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

End point timeframe:

At Week 24

| End point values | Placebo (Weekly infusion) FAS | Epratuzumab 1200 mg every other week (FAS) | Epratuzumab 600 mg per week (FAS) | |
|-----------------------------------|-------------------------------------|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 249 | 244 | 248 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Responder | 33.7 | 43.0 | 39.1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: The percent of subjects meeting treatment response criteria at Week 12 according to a combined response index

| | |
|---|---|
| End point title | The percent of subjects meeting treatment response criteria at Week 12 according to a combined response index |
| End point description: | |
| Percentages are based on the number of subjects in the relevant treatment group within the Full Analysis Set. The combined response index incorporated criteria for achievement of responder status from the: British Isles Lupus Assessment Group Index (BILAG-2004)- improvement from study entry or no worsening in other organ systems, Systemic Lupus Erythematosus Disease Activity Index (SLEDAI; Version 2000, also known as SLEDAI-2K) - no worsening compared to study entry, physician's global assessment of disease activity(PGA)- no worsening compared to study entry, and concomitant medications- no changes. The Full Analysis Set (FAS) consisted of all subjects in the Randomized Set (RS) who had received at least 1 partial dose of study drug, with the exception of 45 subjects who were randomized at site 071, located in the USA, who were excluded from the FAS. | |
| End point type | Secondary |
| End point timeframe: | |
| At Week 12 | |

| End point values | Placebo (Weekly infusion) FAS | Epratuzumab 1200 mg every other week (FAS) | Epratuzumab 600 mg per week (FAS) | |
|-----------------------------------|-------------------------------------|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 249 | 244 | 248 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Responder | 31.3 | 42.2 | 39.9 | |

Statistical analyses

No statistical analyses for this end point

Secondary: The percent of subjects meeting treatment response criteria at Week 36 according to a combined response index

| | |
|---|---|
| End point title | The percent of subjects meeting treatment response criteria at Week 36 according to a combined response index |
| End point description: | |
| Percentages are based on the number of subjects in the relevant treatment group within the Full Analysis Set. The combined response index incorporated criteria for achievement of responder status from the: British Isles Lupus Assessment Group Index (BILAG-2004)- improvement from study entry or no worsening in other organ systems, Systemic Lupus Erythematosus Disease Activity Index (SLEDAI; Version 2000, also known as SLEDAI-2K) - no worsening compared to study entry, physician's global assessment of disease activity(PGA)- no worsening compared to study entry, and concomitant medications- no changes. The Full Analysis Set (FAS) consisted of all subjects in the Randomized Set (RS) who had received at least 1 partial dose of study drug, with the exception of 45 subjects who were randomized at site 071, located in the USA, who were excluded from the FAS. | |
| End point type | Secondary |
| End point timeframe: | |
| At Week 36 | |

| End point values | Placebo (Weekly infusion) FAS | Epratuzumab 1200 mg every other week (FAS) | Epratuzumab 600 mg per week (FAS) | |
|-----------------------------------|-------------------------------------|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 249 | 244 | 248 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Responder | 33.3 | 41.8 | 35.1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in daily corticosteroid dose at week 24

| | |
|---|--|
| End point title | Change from Baseline in daily corticosteroid dose at week 24 |
| End point description: | |
| Subjects with a missing corticosteroid dose at any visit for any reason are counted in the Dose Increased or Missing Data category for that visit. The Full Analysis Set (FAS) consisted of all subjects in the Randomized Set (RS) who had received at least 1 partial dose of study drug, with the exception of 45 subjects who were randomized at site 071, located in the USA, who were excluded from the FAS. | |
| End point type | Secondary |
| End point timeframe: | |
| At Week 24 | |

| End point values | Placebo (Weekly infusion) FAS | Epratuzumab 1200 mg every other week (FAS) | Epratuzumab 600 mg per week (FAS) | |
|-----------------------------------|-------------------------------------|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 249 | 244 | 248 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Dose decreased by >50% | 9.2 | 8.2 | 6.9 | |
| Dose decreased >0% to <=50% | 10.8 | 16.4 | 14.9 | |
| No change in dose | 52.2 | 50.0 | 50.8 | |
| Dose increased or missing data | 27.7 | 25.4 | 27.4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in daily corticosteroid dose at week 48

| | |
|---|--|
| End point title | Change from Baseline in daily corticosteroid dose at week 48 |
| End point description: | |
| Subjects with a missing corticosteroid dose at any visit for any reason are counted in the Dose | |

Increased or Missing Data category for that visit.

The Full Analysis Set (FAS) consisted of all subjects in the Randomized Set (RS) who had received at least 1 partial dose of study drug, with the exception of 45 subjects who were randomized at site 071, located in the USA, who were excluded from the FAS.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Week 48 | |

| End point values | Placebo (Weekly infusion) FAS | Epratuzumab 1200 mg every other week (FAS) | Epratuzumab 600 mg per week (FAS) | |
|-----------------------------------|-------------------------------------|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 249 | 244 | 248 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Dose decreased by >50% | 14.1 | 11.9 | 10.1 | |
| Dose decreased >0% to ≤50% | 10.4 | 14.3 | 12.5 | |
| No change in dose | 38.6 | 37.7 | 37.9 | |
| Dose increased or missing data | 36.9 | 36.1 | 39.5 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

TEAEs were collected throughout the study (on or after first infusion of study drug and within 75 days of the last infusion), for an average of 4.4 years (starting in December 2010 and concluding in May 2015). The SS will be utilized for TEAE reporting.

Adverse event reporting additional description:

The Safety Set consisted of all enrolled subjects who took at least 1 dose of study drug.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 17 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Placebo (Weekly infusion) |
|-----------------------|---------------------------|

Reporting group description:

Placebo infusions delivered weekly for a total of 4 weeks over four 12-week treatment cycles

| | |
|-----------------------|-----------------------------|
| Reporting group title | Epratuzumab 600 mg per week |
|-----------------------|-----------------------------|

Reporting group description:

600 mg infusions delivered weekly for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Epratuzumab 1200 mg every other week |
|-----------------------|--------------------------------------|

Reporting group description:

1200 mg infusions delivered every other week for a total of 4 weeks (cumulative dose 2400 mg) over four 12-week treatment cycles and placebo infusions delivered every other week for a total of 4 weeks over four 12-week treatment cycles

| Serious adverse events | Placebo (Weekly infusion) | Epratuzumab 600 mg per week | Epratuzumab 1200 mg every other week |
|---|---------------------------|-----------------------------|--------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 48 / 263 (18.25%) | 45 / 264 (17.05%) | 44 / 259 (16.99%) |
| number of deaths (all causes) | 1 | 2 | 2 |
| number of deaths resulting from adverse events | 1 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon adenoma | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Ovarian adenoma | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 2 / 264 (0.76%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteriosclerosis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Jugular vein thrombosis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Lupus vasculitis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Surgical and medical procedures | | | |
| Abortion induced | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |

| | | | |
|--|-----------------|-----------------|-----------------|
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 2 / 263 (0.76%) | 2 / 264 (0.76%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inflammation | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 2 / 263 (0.76%) | 0 / 264 (0.00%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serositis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 1 / 264 (0.38%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serum sickness | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Reproductive system and breast disorders | | | |
| Breast ulceration | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Endometriosis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Ovarian cyst ruptured | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| 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 | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 2 / 264 (0.76%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary alveolar haemorrhage | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 2 / 259 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Asthma | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Psychiatric disorders | | | |
| Delirium tremens | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Bipolar I disorder | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Depression | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Femoral neck fracture | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Fibula fracture | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 fracture | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Congenital, familial and genetic disorders | | | |
| Arteriovenous malformation | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Cerebrovascular arteriovenous malformation | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericarditis lupus | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Convulsion | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 263 (0.38%) | 1 / 264 (0.38%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 1 / 264 (0.38%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Carotid artery thrombosis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Lupus encephalitis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Partial seizures with secondary generalisation | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Mononeuropathy multiplex | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 2 / 264 (0.76%) | 2 / 259 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Splenomegaly | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Eye disorders | | | |
| Retinal detachment | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 3 / 264 (1.14%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mesenteric artery thrombosis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bezoar | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 1 / 264 (0.38%) | 2 / 259 (0.77%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lupus hepatitis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Cutaneous lupus erythematosus | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Hidradenitis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Swelling face | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Renal and urinary disorders | | | |
| Lupus nephritis | | | |
| subjects affected / exposed | 2 / 263 (0.76%) | 1 / 264 (0.38%) | 2 / 259 (0.77%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 2 / 259 (0.77%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 failure acute | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Urinary retention | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 263 (0.76%) | 0 / 264 (0.00%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Hyperparathyroidism | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Systemic lupus erythematosus | | | |
| subjects affected / exposed | 3 / 263 (1.14%) | 3 / 264 (1.14%) | 5 / 259 (1.93%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Costochondritis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemarthrosis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoporotic fracture | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Back pain | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Cervical spinal stenosis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Infections and infestations | | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 3 / 264 (1.14%) | 3 / 259 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 2 / 264 (0.76%) | 3 / 259 (1.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 4 / 264 (1.52%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 263 (1.52%) | 2 / 264 (0.76%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 3 / 4 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess neck | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial pyelonephritis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Herpes zoster meningitis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Localised infection | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphangitis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myringitis bullous | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Pelvic inflammatory disease | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis chronic | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyomyositis | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 0 / 264 (0.00%) | 1 / 259 (0.39%) |
| 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 shock | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Urinary tract infection pseudomonal | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Pneumococcal sepsis | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 263 (0.38%) | 0 / 264 (0.00%) | 0 / 259 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Obesity | | | |
| subjects affected / exposed | 0 / 263 (0.00%) | 1 / 264 (0.38%) | 0 / 259 (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 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 2 / 263 (0.76%) | 0 / 264 (0.00%) | 0 / 259 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | Placebo (Weekly infusion) | Epratuzumab 600 mg per week | Epratuzumab 1200 mg every other week |
|---|---------------------------|-----------------------------|--------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 144 / 263 (54.75%) | 141 / 264 (53.41%) | 153 / 259 (59.07%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 11 / 263 (4.18%) | 13 / 264 (4.92%) | 20 / 259 (7.72%) |
| occurrences (all) | 12 | 14 | 21 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 29 / 263 (11.03%) | 38 / 264 (14.39%) | 34 / 259 (13.13%) |
| occurrences (all) | 38 | 58 | 42 |
| Dizziness | | | |
| subjects affected / exposed | 11 / 263 (4.18%) | 16 / 264 (6.06%) | 9 / 259 (3.47%) |
| occurrences (all) | 11 | 18 | 10 |
| Migraine | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 3 / 263 (1.14%) 4 | 7 / 264 (2.65%) 8 | 16 / 259 (6.18%) 19 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 10 / 263 (3.80%) 10 | 12 / 264 (4.55%) 17 | 17 / 259 (6.56%) 20 |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) | 23 / 263 (8.75%) 28 17 / 263 (6.46%) 19 | 38 / 264 (14.39%) 49 19 / 264 (7.20%) 28 | 30 / 259 (11.58%) 44 21 / 259 (8.11%) 24 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 12 / 263 (4.56%) 16 | 12 / 264 (4.55%) 12 | 13 / 259 (5.02%) 14 |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 5 / 263 (1.90%) 5 | 8 / 264 (3.03%) 8 | 14 / 259 (5.41%) 16 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all) | 14 / 263 (5.32%) 21 10 / 263 (3.80%) 14 11 / 263 (4.18%) 13 | 14 / 264 (5.30%) 24 15 / 264 (5.68%) 17 9 / 264 (3.41%) 9 | 20 / 259 (7.72%) 28 19 / 259 (7.34%) 20 14 / 259 (5.41%) 18 |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection | 30 / 263 (11.41%) 36 | 32 / 264 (12.12%) 38 | 32 / 259 (12.36%) 38 |

| | | | |
|-----------------------------|-------------------|-------------------|------------------|
| subjects affected / exposed | 30 / 263 (11.41%) | 27 / 264 (10.23%) | 25 / 259 (9.65%) |
| occurrences (all) | 41 | 41 | 29 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 21 / 263 (7.98%) | 22 / 264 (8.33%) | 20 / 259 (7.72%) |
| occurrences (all) | 26 | 29 | 21 |
| Sinusitis | | | |
| subjects affected / exposed | 13 / 263 (4.94%) | 15 / 264 (5.68%) | 24 / 259 (9.27%) |
| occurrences (all) | 14 | 17 | 24 |
| Bronchitis | | | |
| subjects affected / exposed | 20 / 263 (7.60%) | 15 / 264 (5.68%) | 12 / 259 (4.63%) |
| occurrences (all) | 23 | 18 | 14 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 22 November 2011 | <p>The protocol was amended for the following reasons:</p> <ul style="list-style-type: none">-To change the name & contact information of the Clinical Trial Biostatistician & Study Physician-To add additional exploratory endpoints for assessment of the 36-Item Short Form Health Survey (SF-36) & flares-To clarify the guidance for use of oral corticosteroids for the investigator-To add the sampling time points for overall B & T cell levels during the study & to add a body weight measurement at Wk 48. These were inadvertently omitted from the original protocol-To modify Inclusion Criterion #5 for female subjects to allow abstinence alone & condoms/diaphragm use without adjunct spermicide-To modify Exclusion Criterion #15 to clarify that subjects who had previously received Emab treatment were excluded from participation in this study-To update the withdrawal criteria list: subjects who received a live vaccine during the study must have been withdrawn-To increase the Wash-Out Period for the prohibited concomitant treatment TACI-Ig (Atacicept®) from 3 months to 10 months based on recently reported data. The screening window had been increased from 2 days to 5 days, to allow the Screening Period to be extended after discussion with & approval of the medical monitor if it was in the best interest of the subject, & to allow rescreening of subjects on a case-by-case basis at the discretion of the medical monitor-To add additional details to the description of the SF-36 assessment-To include a list of Anticipated Serious AEs in compliance with the recent US Food & Drug Administration (FDA) guidance on safety reporting requirements for studies conducted under an open Investigational New Drug Application (FDA, Guidance for Industry and Investigators, 2010)-To modify the definition of the Pharmacokinetic Set (PKS) to include the requirement of at least 1 Emab plasma concentration measurement <p>In addition, a few clarifications, inconsistencies, & typographical errors had been made/corrected within the protocol text</p> |

| | |
|-------------|---|
| 09 May 2014 | <p>The protocol was amended at the request of the German Regulatory Authority Paul-Ehrlich-Institut to clarify details of the British Isles Lupus Assessment Group (BILAG) assessment, to introduce a list of AEs of special interest, & to clarify further actions after their identification:</p> <ul style="list-style-type: none"> - Updated study contact information - Updated SAE reporting information - Revised the exploratory endpoints for assessment of flares & for assessment of the Systemic Lupus International Collaborating/American College of Rheumatology (SLICC/ACR) Damage score - Added an additional safety variable (incidence of hospitalizations/emergency room visits) - Clarified the guidance for use of oral corticosteroids for the investigator to note that subjects with increases in oral corticosteroids above the allowed levels for an SLE-related indication are considered nonresponders - Corrected the visit numbers cited in Exclusion Criterion #14 - Updated Steroid conversion table with additional corticosteroids - Updated the text "Preparation & administration of Emab and placebo" to clarify that it is recommended, but not mandatory, that subjects be premedicated before receiving an iv infusion - Updated the text "Handling & storage requirements" to clarify the process to follow in case of out-of-range temperatures - Updated the version number of the European Quality of Life-5 Dimensions questionnaire to European Quality of Life-5 Dimensions 3 level version - Modified the generalized estimating equation (GEE) sensitivity analysis to avoid known violations of the missing completely at random assumption, & to be consistent with the current Statistical Analysis Plan (SAP). The original plan for assessing the impact of missing data on the primary endpoint has not changed - Modified the text "Safety analyses" to state that infection TEAEs will be identified by including all events in the coded SOC "Infections and infestations" rather than via a review of all AE terms prior to study unblinding, as originally planned |
|-------------|---|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported