



## Clinical trial results:

### A Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging, Parallel-Group, Phase 2b Study of LY3009104 in Patients with Active Rheumatoid Arthritis on Background Methotrexate Therapy

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2010-022504-42 |
| Trial protocol           | GB HU          |
| Global end of trial date | 31 March 2014  |

#### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)                                       |
| This version publication date  | 14 October 2017                                    |
| First version publication date | 26 March 2017                                      |
| Version creation reason        | • Correction of full data set<br>Revision Required |

#### Trial information

##### Trial identification

|                       |       |
|-----------------------|-------|
| Sponsor protocol code | 13854 |
|-----------------------|-------|

##### Additional study identifiers

|                                    |   |
|------------------------------------|---|
| ISRCTN number                      | -   |
| ClinicalTrials.gov id (NCT number) | NCT01185353                               |
| WHO universal trial number (UTN)   | -   |
| Other trial identifiers            | Trial Alias: I4V-MC-JADA, Trial ID: 13854 |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Eli Lilly and Company   |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, United States, 46285                  |
| Public contact               | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLilly,  |
| Scientific contact           | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559, |

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                       | 31 March 2014 |
| Is this the analysis of the primary completion data? | No            |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 31 March 2014 |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this trial is to evaluate the safety and efficacy of LY3009104 in participants with Rheumatoid Arthritis (RA).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy:

Methotrexate (MTX) was administered orally as background therapy. Participants must have regularly used methotrexate (MTX) for at least 12 weeks, with treatment at a stable dose of 10 to 25 milligrams (mg) per week for at least 8 weeks prior to baseline.

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 13 October 2010 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 95  |
| Country: Number of subjects enrolled | Hungary: 13        |
| Country: Number of subjects enrolled | Czech Republic: 23 |
| Country: Number of subjects enrolled | Mexico: 47         |
| Country: Number of subjects enrolled | Poland: 33         |
| Country: Number of subjects enrolled | Ukraine: 29        |
| Country: Number of subjects enrolled | Croatia: 7         |
| Country: Number of subjects enrolled | Romania: 11        |
| Country: Number of subjects enrolled | India: 43          |
| Worldwide total number of subjects   | 301                |
| EEA total number of subjects         | 87                 |

Notes:

### Subjects enrolled per age group

|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |     |
|--|-----|
| wk                                       |     |
| 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)                     | 263 |
| From 65 to 84 years                      | 38  |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

This study consisted of 4 parts and a follow-up up to 28 days post the last dose of study drug.

### Period 1

|                              |                             |
|------------------------------|-----------------------------|
| Period 1 title               | Part A (Weeks 0 through 12) |
| Is this the baseline period? | Yes                         |
| Allocation method            | Randomised - controlled     |
| Blinding used                | Double blind                |
| Roles blinded                | Subject, Investigator       |

### Arms

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

|                  |  |
|------------------|--|
| <b>Arm title</b> | 1 milligram (mg) LY3009104 QD - Part A |
|------------------|--|

Arm description:

Administered orally once daily (QD) for 12 weeks in Part A.

Methotrexate (MTX) was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

Dosage and administration details:

1mg LY3009104 once daily for 12 weeks in Part A

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | 2 mg LY3009104 QD - Parts A and B |
|------------------|-----------------------------------|

Arm description:

Administered orally QD for 24 weeks in Parts A and B.

MTX was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

Dosage and administration details:

2 mg LY3009104 once daily for 24 weeks in Parts A and B

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | 4 mg LY3009104 QD - Parts A and B |
|------------------|-----------------------------------|

Arm description:

Administered orally QD for 24 weeks in Parts A and B.

MTX was administered orally as background therapy.

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

|   |   |
|---|---|
| Investigational medicinal product name                  | Baricitinib   |
| Investigational medicinal product code                  | LY3009104   |
| Other name  | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                                    | Capsule   |
| Routes of administration                                | Oral use  |
| Dosage and administration details:                      |   |
| 4 mg LY3009104 once daily for 24 weeks in Parts A and B |   |
| <b>Arm title</b>  | 8 mg LY3009104 QD - Parts A and B                       |

Arm description:

Administered orally QD for 24 weeks in Parts A and B.

MTX was administered orally as background therapy.

|   |   |
|---|---|
| Arm type  | Experimental  |
| Investigational medicinal product name                  | Baricitinib   |
| Investigational medicinal product code                  | LY3009104   |
| Other name  | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                                    | Capsule   |
| Routes of administration                                | Oral use  |
| Dosage and administration details:                      |   |
| 8 mg LY3009104 once daily for 24 weeks in Parts A and B |   |
| <b>Arm title</b>  | Placebo QD - Part A                                     |

Arm description:

Placebo administered orally QD for 12 weeks in Part A.

MTX was administered orally as background therapy.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Placebo      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Placebo daily for 12 weeks

| <b>Number of subjects in period 1</b>  | 1 milligram (mg)<br>LY3009104 QD -<br>Part A | 2 mg LY3009104 QD<br>- Parts A and B | 4 mg LY3009104 QD<br>- Parts A and B |
|--|--|--------------------------------------|--------------------------------------|
| Started                                | 49   | 52                                   | 52                                   |
| Received at least 1 dose of study drug | 49   | 52                                   | 52                                   |
| Completed                              | 44   | 51                                   | 50                                   |
| Not completed                          | 5  | 1                                    | 2                                    |
| Consent withdrawn by subject           | 2  | -                                    | -                                    |
| Physician decision                     | -  | -                                    | 1                                    |
| Adverse event, non-fatal               | 1  | 1                                    | 1                                    |
| Entry Criteria Not Met                 | -  | -                                    | -                                    |
| Lack of efficacy                       | 2  | -                                    | -                                    |
| Protocol deviation                     | -  | -                                    | -                                    |

| <b>Number of subjects in period 1</b>  | <b>8 mg LY3009104 QD<br/>- Parts A and B</b> | <b>Placebo QD - Part A</b> |
|--|--|----------------------------|
| Started                                | 50   | 98                         |
| Received at least 1 dose of study drug | 50   | 98                         |
| Completed                              | 49   | 82                         |
| Not completed                          | 1  | 16                         |
| Consent withdrawn by subject           | -  | 3                          |
| Physician decision                     | -  | 2                          |
| Adverse event, non-fatal               | 1  | 5                          |
| Entry Criteria Not Met                 | -  | 4                          |
| Lack of efficacy                       | -  | 1                          |
| Protocol deviation                     | -  | 1                          |

## Period 2

|                              |                              |
|------------------------------|------------------------------|
| Period 2 title               | Part B (Weeks 12 through 24) |
| Is this the baseline period? | No                           |
| Allocation method            | Randomised - controlled      |
| Blinding used                | Double blind                 |
| Roles blinded                | Subject, Investigator        |

## Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes                                      |
| <b>Arm title</b>             | <b>2 mg LY3009104 QD - Parts A and B</b> |

Arm description:

Administered orally QD for 24 weeks in Parts A and B.

MTX was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

Dosage and administration details:

2 mg LY3009104 once daily for 24 weeks in Parts A and B

|                  |  |
|------------------|--|
| <b>Arm title</b> | <b>4 mg LY3009104 QD - Parts A and B</b> |
|------------------|--|

Arm description:

Administered orally QD for 24 weeks in Parts A and B.

MTX was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

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**Dosage and administration details:**

4 mg LY3009104 once daily for 24 weeks in Parts A and B

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | 8 mg LY3009104 QD - Parts A and B |
|------------------|-----------------------------------|

**Arm description:**

Administered orally QD for 24 weeks in Parts A and B.

MTX was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

**Dosage and administration details:**

8 mg LY3009104 once daily for 24 weeks in Parts A and B

|                  |                             |
|------------------|-----------------------------|
| <b>Arm title</b> | 2 mg LY3009104 BID - Part B |
|------------------|-----------------------------|

**Arm description:**

Participants who received Placebo or 1 mg LY3009104 in Part A were re-randomized at Week 12 to receive 2 mg LY3009104 twice daily (BID) in Part B.

MTX was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

**Dosage and administration details:**

2 mg LY3009104 twice daily for 12 weeks in Part B

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | 4 mg LY3009104 QD - Part B |
|------------------|----------------------------|

**Arm description:**

Participants who received Placebo or 1 mg LY3009104 in Part A were re-randomized at Week 12 to receive 4 mg LY3009104 QD in Part B.

MTX was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

**Dosage and administration details:**

4 mg LY3009104 once daily for 12 weeks in Part B

| <b>Number of subjects in period 2</b> | 2 mg LY3009104 QD<br>- Parts A and B | 4 mg LY3009104 QD<br>- Parts A and B | 8 mg LY3009104 QD<br>- Parts A and B |
|---------------------------------------|--------------------------------------|--------------------------------------|--------------------------------------|
| Started                               | 51                                   | 50                                   | 49                                   |
| Completed                             | 50                                   | 48                                   | 45                                   |
| Not completed                         | 1                                    | 2                                    | 4                                    |
| Consent withdrawn by subject          | -                                    | 1                                    | 2                                    |
| Adverse event, non-fatal              | -                                    | 1                                    | -                                    |
| Lost to follow-up                     | -                                    | -                                    | 1                                    |
| Entry Criteria Not Met                | -                                    | -                                    | -                                    |
| Lack of efficacy                      | 1                                    | -                                    | 1                                    |

| <b>Number of subjects in period 2</b> | 2 mg LY3009104<br>BID - Part B | 4 mg LY3009104 QD<br>- Part B |
|---------------------------------------|--------------------------------|-------------------------------|
| Started                               | 63                             | 63                            |
| Completed                             | 59                             | 57                            |
| Not completed                         | 4                              | 6                             |
| Consent withdrawn by subject          | 3                              | 4                             |
| Adverse event, non-fatal              | 1                              | -                             |
| Lost to follow-up                     | -                              | 1                             |
| Entry Criteria Not Met                | -                              | 1                             |
| Lack of efficacy                      | -                              | -                             |

### Period 3

|                              |                              |
|------------------------------|------------------------------|
| Period 3 title               | Part C (Weeks 24 through 76) |
| Is this the baseline period? | No                           |
| Allocation method            | Non-randomised - controlled  |
| Blinding used                | Not blinded                  |

### Arms

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| <b>Arm title</b>             | 4 mg LY3009104 QD - Parts C and D |

#### Arm description:

Participants who received 2 mg LY3009104 QD or BID in Part B were re-assigned at Week 24 to 4 mg LY3009104 QD in Part C.

Participants who received 4 mg LY3009104 QD in Part B continued to receive 4 mg LY3009104 QD in Part C.

Participants who completed Part C continued to receive 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.

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



|  |  |
|--|--|
| Investigational medicinal product name   | Baricitinib  |
| Investigational medicinal product code   | LY3009104  |
| Other name   | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050        |
| Pharmaceutical forms   | Capsule  |
| Routes of administration   | Oral use   |
| Dosage and administration details:<br>4 mg LY3009104 once daily for 52 weeks in Part C |  |
| <b>Arm title</b>   | 4 to 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D |

Arm description:

Participants who received 2 mg LY3009104 QD or BID in Part B were re-assigned at Week 24 to 4 mg LY3009104 QD in Part C.

Participants who received 4 mg LY3009104 QD in Part B continued to receive 4 mg LY3009104 QD in Part C.

At Weeks 28 and 32, participants who met dose escalation criteria received 8 mg LY3009104 QD for the rest of Part C.

Dose escalation criteria:  $\geq 6$  tender and 6 swollen joints based on the 28-joint count assessments and the clinical judgment of the investigator.

Participants who completed Part C received 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.

|   |   |
|---|---|
| Arm type  | Experimental  |
| Investigational medicinal product name  | Baricitinib   |
| Investigational medicinal product code  | LY3009104   |
| Other name  | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050   |
| Pharmaceutical forms  | Capsule   |
| Routes of administration  | Oral use  |
| Dosage and administration details:<br>4mg escalated to 8 mg LY3009104 once daily for 52 weeks in Part C |   |
| <b>Arm title</b>  | 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D |

Arm description:

Participants who received 8 mg LY3009104 QD in Part B remained on 8 mg LY3009104 QD in Part C.

Participants who completed Part C received 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

Dosage and administration details:

8 mg LY3009104 once daily for 52 weeks in Part C

| Number of subjects in period 3 <sup>[1]</sup> | 4 mg LY3009104 QD<br>- Parts C and D | 4 to 8 mg<br>LY3009104 QD -<br>Part C and 4 mg<br>LY3009104 QD -<br>Part D | 8 mg LY3009104 QD<br>- Part C and 4 mg<br>LY3009104 QD -<br>Part D |
|---|--------------------------------------|--|--|
|   |                                      |  |  |
| Started                                       | 108                                  | 61   | 32   |
| Completed                                     | 92                                   | 53   | 24   |
| Not completed                                 | 16                                   | 8  | 8  |
| Adverse event, serious fatal                  | -                                    | -  | 1  |
| Consent withdrawn by subject                  | 6                                    | 2  | 2  |
| Physician decision                            | -                                    | -  | 1  |
| Adverse event, non-fatal                      | 8                                    | 2  | 2  |
| Lost to follow-up                             | 2                                    | 1  | 1  |
| Entry Criteria Not Met                        | -                                    | -  | 1  |
| Reason missing                                | -                                    | 1  | -  |
| Lack of efficacy                              | -                                    | 2  | -  |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Participants who received 2mg LY3009104 QD or BID in Part B were reassigned at Wk 24 to receive 4 mg LY3009104 in Part C. Participants who received 4mg LY3009104 in Part B continued to receive 4mg LY3009104 in Part C. At Wk 28 participants were assessed for dose escalation to receive 8 mg LY3009104 QD for the remainder of Part C. Participants who received 8 mg LY3009104 QD in Part B remained on 8 mg LY3009104 QD in Part C.

**Period 4**

|                              |                               |
|------------------------------|-------------------------------|
| Period 4 title               | Part D (Weeks 76 through 128) |
| Is this the baseline period? | No                            |
| Allocation method            | Non-randomised - controlled   |
| Blinding used                | Not blinded                   |

**Arms**

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| <b>Arm title</b>             | 4 mg LY3009104 QD - Parts C and D |

Arm description:

Participants who received 2 mg LY3009104 QD or BID in Part B were re-assigned at Week 24 to 4 mg LY3009104 QD in Part C.

Participants who received 4 mg LY3009104 QD in Part B continued to receive 4 mg LY3009104 QD in Part C.

Participants who completed Part C continued to receive 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

Dosage and administration details:

4 mg LY3009104 once daily for 52 weeks in Part D

|                  |  |
|------------------|--|
| <b>Arm title</b> | 4 to 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D |
|------------------|--|

Arm description:

Participants who received 2 mg LY3009104 QD or BID in Part B were re-assigned at Week 24 to 4 mg LY3009104 QD in Part C.

Participants who received 4 mg LY3009104 QD in Part B continued to receive 4 mg LY3009104 QD in Part C.

At Weeks 28 and 32, participants who met dose escalation criteria received 8 mg LY3009104 QD for the rest of Part C.

Dose escalation criteria:  $\geq 6$  tender and 6 swollen joints based on the 28-joint count assessments and the clinical judgment of the investigator.

Participants who completed Part C received 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

Dosage and administration details:

4 mg LY3009104 once daily for 52 weeks in Part D

|                  |   |
|------------------|---|
| <b>Arm title</b> | 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D |
|------------------|---|

Arm description:

Participants who received 8 mg LY3009104 QD in Part B remained on 8 mg LY3009104 QD in Part C.

Participants who completed Part C received 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.

|  |   |
|--|---|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Baricitinib   |
| Investigational medicinal product code | LY3009104   |
| Other name                             | Janus Kinase (JAK)1/JAK2, JAK 1/2 Inhibitor, INCB028050 |
| Pharmaceutical forms                   | Capsule   |
| Routes of administration               | Oral use  |

Dosage and administration details:

4 mg LY3009104 once daily for 52 weeks in Part D

| Number of subjects in period 4[2] | 4 mg LY3009104 QD - Parts C and D | 4 to 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D | 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D |
|-----------------------------------|-----------------------------------|--|---|
|                                   |                                   |  |   |
| Started                           | 79                                | 47   | 18  |
| Completed                         | 76                                | 40   | 17  |
| Not completed                     | 3                                 | 7  | 1   |
| Consent withdrawn by subject      | 1                                 | 2  | 1   |
| Adverse event, non-fatal          | 1                                 | 2  | -   |
| Lost to follow-up                 | 1                                 | 3  | -   |

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Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Participants who completed Part C received 4 mg LY3009104 QD in Part D regardless of dose in Parts B and C.

## Baseline characteristics

### Reporting groups

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Part A (Weeks 0 through 12) |
|-----------------------|-----------------------------|

Reporting group description: -

| Reporting group values                             | Part A (Weeks 0 through 12) | Total |  |
|--|-----------------------------|-------|--|
| Number of subjects                                 | 301                         | 301   |  |
| Age categorical                                    |                             |       |  |
| Units: Subjects                                    |                             |       |  |
| In utero   | 0                           | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                           | 0     |  |
| Newborns (0-27 days)                               | 0                           | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0                           | 0     |  |
| Children (2-11 years)                              | 0                           | 0     |  |
| Adolescents (12-17 years)                          | 0                           | 0     |  |
| Adults (18-64 years)                               | 263                         | 263   |  |
| From 65-84 years                                   | 38                          | 38    |  |
| 85 years and over                                  | 0                           | 0     |  |
| Age Continuous                                     |                             |       |  |
| Units: years                                       |                             |       |  |
| arithmetic mean                                    | 51.2                        |       |  |
| standard deviation                                 | ± 11.71                     | -     |  |
| Gender, Male/Female                                |                             |       |  |
| Units: participants                                |                             |       |  |
| Female   | 249                         | 249   |  |
| Male   | 52                          | 52    |  |
| Ethnicity (NIH/OMB)                                |                             |       |  |
| Units: Subjects                                    |                             |       |  |
| Hispanic or Latino                                 | 56                          | 56    |  |
| Not Hispanic or Latino                             | 227                         | 227   |  |
| Unknown or Not Reported                            | 18                          | 18    |  |
| Race (NIH/OMB)                                     |                             |       |  |
| Units: Subjects                                    |                             |       |  |
| American Indian or Alaska Native                   | 19                          | 19    |  |
| Asian  | 47                          | 47    |  |
| Native Hawaiian or Other Pacific Islander          | 0                           | 0     |  |
| Black or African American                          | 11                          | 11    |  |
| White  | 224                         | 224   |  |
| More than one race                                 | 0                           | 0     |  |
| Unknown or Not Reported                            | 0                           | 0     |  |
| Region of Enrollment                               |                             |       |  |
| Units: Subjects                                    |                             |       |  |
| United States                                      | 95                          | 95    |  |
| Hungary  | 13                          | 13    |  |
| Czech Republic                                     | 23                          | 23    |  |

|  |          |    |  |
|--|----------|----|--|
| Mexico   | 47       | 47 |  |
| Poland   | 33       | 33 |  |
| Ukraine  | 29       | 29 |  |
| Croatia  | 7        | 7  |  |
| Romania  | 11       | 11 |  |
| India  | 43       | 43 |  |
| Duration of Rheumatoid Arthritis   |          |    |  |
| Units: years   |          |    |  |
| arithmetic mean  | 5.62     |    |  |
| standard deviation   | ± 4.401  | -  |  |
| Tender Joint Counts (TJC)  |          |    |  |
| TJC is the number of tender and painful joints determined for each participant by examination of 68 joints. Joints were assessed by pressure and joint manipulation on physical examination. Participants were asked for pain sensations on these manipulations and watched for spontaneous pain reactions. Any positive response on pressure, movement, or both was translated into a single tender-versus-nontender dichotomy. |          |    |  |
| Units: number of joints  |          |    |  |
| arithmetic mean  | 22.2     |    |  |
| standard deviation   | ± 12.38  | -  |  |
| Swollen Joint Counts (SJC)   |          |    |  |
| SJC is the number of swollen joints determined for each participant by examination of 66 joints. Joints were classified as either swollen or not swollen. Swelling was defined as palpable fluctuating synovitis of the joint.   |          |    |  |
| Units: number of joints  |          |    |  |
| arithmetic mean  | 15.8     |    |  |
| standard deviation   | ± 8.13   | -  |  |
| High Sensitivity C-Reactive Protein (hsCRP)  |          |    |  |
| HsCRP is a laboratory analyte that is an indicator of inflammation. Decreases in hsCRP represent reductions in inflammation. Numbers of participants analyzed are 49, 52, 52, 50 for 1 mg, 2 mg, 4 mg, and 8 mg LY3009104 groups respectively, and 97 for placebo group.   |          |    |  |
| Units: milligrams/liter (mg/L)   |          |    |  |
| arithmetic mean  | 12.81    |    |  |
| standard deviation   | ± 19.402 | -  |  |
| Erythrocyte Sedimentation Rate (ESR)   |          |    |  |
| ESR is a laboratory analyte that is an indicator of inflammation. Decreases represent reductions in inflammation.  |          |    |  |
| Units: millimeters/hour (mm/hr)  |          |    |  |
| arithmetic mean  | 38.8     |    |  |
| standard deviation   | ± 18.39  | -  |  |

## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | 1 milligram (mg) LY3009104 QD - Part A |
| Reporting group description:<br>Administered orally once daily (QD) for 12 weeks in Part A.<br><br>Methotrexate (MTX) was administered orally as background therapy.   |  |
| Reporting group title  | 2 mg LY3009104 QD - Parts A and B      |
| Reporting group description:<br>Administered orally QD for 24 weeks in Parts A and B.<br><br>MTX was administered orally as background therapy.  |  |
| Reporting group title  | 4 mg LY3009104 QD - Parts A and B      |
| Reporting group description:<br>Administered orally QD for 24 weeks in Parts A and B.<br><br>MTX was administered orally as background therapy.  |  |
| Reporting group title  | 8 mg LY3009104 QD - Parts A and B      |
| Reporting group description:<br>Administered orally QD for 24 weeks in Parts A and B.<br><br>MTX was administered orally as background therapy.  |  |
| Reporting group title  | Placebo QD - Part A                    |
| Reporting group description:<br>Placebo administered orally QD for 12 weeks in Part A.<br><br>MTX was administered orally as background therapy.   |  |
| Reporting group title  | 2 mg LY3009104 QD - Parts A and B      |
| Reporting group description:<br>Administered orally QD for 24 weeks in Parts A and B.<br><br>MTX was administered orally as background therapy.  |  |
| Reporting group title  | 4 mg LY3009104 QD - Parts A and B      |
| Reporting group description:<br>Administered orally QD for 24 weeks in Parts A and B.<br><br>MTX was administered orally as background therapy.  |  |
| Reporting group title  | 8 mg LY3009104 QD - Parts A and B      |
| Reporting group description:<br>Administered orally QD for 24 weeks in Parts A and B.<br><br>MTX was administered orally as background therapy.  |  |
| Reporting group title  | 2 mg LY3009104 BID - Part B            |
| Reporting group description:<br>Participants who received Placebo or 1 mg LY3009104 in Part A were re-randomized at Week 12 to receive 2 mg LY3009104 twice daily (BID) in Part B.<br><br>MTX was administered orally as background therapy. |  |
| Reporting group title  | 4 mg LY3009104 QD - Part B             |
| Reporting group description:<br>Participants who received Placebo or 1 mg LY3009104 in Part A were re-randomized at Week 12 to receive 4 mg LY3009104 QD in Part B.<br><br>MTX was administered orally as background therapy.                |  |
| Reporting group title  | 4 mg LY3009104 QD - Parts C and D      |

Reporting group description:

Participants who received 2 mg LY3009104 QD or BID in Part B were re-assigned at Week 24 to 4 mg LY3009104 QD in Part C.

Participants who received 4 mg LY3009104 QD in Part B continued to receive 4 mg LY3009104 QD in Part C.

Participants who completed Part C continued to receive 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.

|                       |  |
|-----------------------|--|
| Reporting group title | 4 to 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D |
|-----------------------|--|

Reporting group description:

Participants who received 2 mg LY3009104 QD or BID in Part B were re-assigned at Week 24 to 4 mg LY3009104 QD in Part C.

Participants who received 4 mg LY3009104 QD in Part B continued to receive 4 mg LY3009104 QD in Part C.

At Weeks 28 and 32, participants who met dose escalation criteria received 8 mg LY3009104 QD for the rest of Part C.

Dose escalation criteria:  $\geq 6$  tender and 6 swollen joints based on the 28-joint count assessments and the clinical judgment of the investigator.

Participants who completed Part C received 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.

|                       |   |
|-----------------------|---|
| Reporting group title | 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D |
|-----------------------|---|

Reporting group description:

Participants who received 8 mg LY3009104 QD in Part B remained on 8 mg LY3009104 QD in Part C.

Participants who completed Part C received 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | 4 mg LY3009104 QD - Parts C and D |
|-----------------------|-----------------------------------|

Reporting group description:

Participants who received 2 mg LY3009104 QD or BID in Part B were re-assigned at Week 24 to 4 mg LY3009104 QD in Part C.

Participants who received 4 mg LY3009104 QD in Part B continued to receive 4 mg LY3009104 QD in Part C.

Participants who completed Part C continued to receive 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.

|                       |  |
|-----------------------|--|
| Reporting group title | 4 to 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D |
|-----------------------|--|

Reporting group description:

Participants who received 2 mg LY3009104 QD or BID in Part B were re-assigned at Week 24 to 4 mg LY3009104 QD in Part C.

Participants who received 4 mg LY3009104 QD in Part B continued to receive 4 mg LY3009104 QD in Part C.

At Weeks 28 and 32, participants who met dose escalation criteria received 8 mg LY3009104 QD for the rest of Part C.

Dose escalation criteria:  $\geq 6$  tender and 6 swollen joints based on the 28-joint count assessments and the clinical judgment of the investigator.

Participants who completed Part C received 4 mg LY3009104 QD in Part D.

MTX was administered orally as background therapy.



|  |   |
|--|---|
| Reporting group title  | 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D     |
| Reporting group description:   |   |
| Participants who received 8 mg LY3009104 QD in Part B remained on 8 mg LY3009104 QD in Part C.   |   |
| Participants who completed Part C received 4 mg LY3009104 QD in Part D.  |   |
| MTX was administered orally as background therapy.   |   |
| Subject analysis set title   | Combined 4mg and 8mg ACR20 Response Week 12                   |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:  |   |
| All randomized participants who received placebo, 4 mg or 8 mg LY3009104 in Part A. Participants who had missing components of the ACR20 index at Week 12 had these components imputed by last observation carried forward (LOCF). |   |
| Subject analysis set title   | 4mg ACR20 Response Weeks (Wks) 76 and 128                     |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:  |   |
| All participants who received study drug in Parts C and D. Participants who had missing components of the ACR20 index at analysis time points had these components imputed by LOCF.  |   |
| Subject analysis set title   | 4-8mg ACR20 Response Wks 76 and 128                           |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:  |   |
| All participants who received study drug in Parts C and D. Participants who had missing components of the ACR20 index at analysis time points had these components imputed by LOCF.  |   |
| Subject analysis set title   | 8mg ACR20 Response Wks 76 and 128                             |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:  |   |
| All participants who received study drug in Parts C and D. Participants who had missing components of the ACR20 index at analysis time points had these components imputed by LOCF.  |   |
| Subject analysis set title   | 4mg ACR70 Response Wks 76 and 128                             |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:  |   |
| All participants who received study drug in Parts C and D. Participants who had missing components of the ACR70 index at analysis time points had these components imputed by LOCF.  |   |
| Subject analysis set title   | 4-8mg ACR70 Response Wks 76 and 128                           |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:  |   |
| All participants who received study drug in Parts C and D. Participants who had missing components of the ACR70 index at analysis time points had these components imputed by LOCF.  |   |
| Subject analysis set title   | 8mg ACR70 Response Wks 76 and 128                             |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:  |   |
| All participants who received study drug in Parts C and D. Participants who had missing components of the ACR70 index at analysis time points had these components imputed by LOCF.  |   |
| Subject analysis set title   | 4mg Mean Change TJC and SJC From Baseline To Wks 76 and 128   |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:  |   |
| All participants who received study drug in Parts C and D and had TJC and SJC evaluated at analysis time points. LOCF was used to impute missing post-baseline values.   |   |
| Subject analysis set title   | 4-8mg Mean Change TJC and SJC From Baseline To Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis  |
| Subject analysis set description:  |   |
| All participants who received study drug in Parts C and D and had TJC and SJC evaluated at analysis time points. LOCF was used to impute missing post-baseline values.   |   |
| Subject analysis set title   | 8mg Mean Change TJC and SJC From Baseline To Wks 76 and 128   |

|  |  |
|--|--|
| Subject analysis set type  | Sub-group analysis                                       |
| Subject analysis set description:<br>All participants who received study drug in Parts C and D and had TJC and SJC evaluated at analysis time points. LOCF was used to impute missing post-baseline values.  |  |
| Subject analysis set title   | 4mg Mean Change HAQ-DI From Baseline To Wks 76 and 128   |
| Subject analysis set type  | Sub-group analysis                                       |
| Subject analysis set description:<br>All participants who received study drug in Parts C and D and had HAQ-DI evaluated at analysis time points. LOCF was used to impute missing post-baseline values  |  |
| Subject analysis set title   | 4-8mg Mean Change HAQ-DI From Baseline To Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis                                       |
| Subject analysis set description:<br>All participants who received study drug in Parts C and D and had HAQ-DI evaluated at analysis time points. LOCF was used to impute missing post-baseline values.   |  |
| Subject analysis set title   | 8mg Mean Change HAQ-DI From Baseline To Wks 76 and 128   |
| Subject analysis set type  | Sub-group analysis                                       |
| Subject analysis set description:<br>All participants who received study drug in Parts C and D and had HAQ-DI evaluated at analysis time points. LOCF was used to impute missing post-baseline values.   |  |
| Subject analysis set title   | 4mg Mean Change hsCRP From Baseline To Wks 76 and 128    |
| Subject analysis set type  | Sub-group analysis                                       |
| Subject analysis set description:<br>All participants who received study drug in Parts C and D and had hsCRP evaluated at analysis time points. LOCF was used to impute missing post-baseline values.  |  |
| Subject analysis set title   | 4-8mg Mean Change hsCRP From Baseline To Wks 76 and 128  |
| Subject analysis set type  | Sub-group analysis                                       |
| Subject analysis set description:<br>All participants who received study drug in Parts C and D and had hsCRP evaluated at analysis time points. LOCF was used to impute missing post-baseline values.  |  |
| Subject analysis set title   | 8mg Mean Change hsCRP From Baseline To Wks 76 and 128    |
| Subject analysis set type  | Sub-group analysis                                       |
| Subject analysis set description:<br>All participants who received study drug in Parts C and D and had hsCRP evaluated at analysis time points. LOCF was used to impute missing post-baseline values.  |  |
| Subject analysis set title   | 4mg DA Assessment Wks 76 and 128                         |
| Subject analysis set type  | Sub-group analysis                                       |
| Subject analysis set description:<br>All participants who received study drug in Parts C and D and had physician's and participant's assessments of disease activity and pain evaluated at analysis time points. LOCF was used to impute missing post-baseline values. |  |
| Subject analysis set title   | 4-8mg DA Assessment Wks 76 and 128                       |
| Subject analysis set type  | Sub-group analysis                                       |
| Subject analysis set description:<br>All participants who received study drug in Parts C and D and had physician's and participant's assessments of disease activity and pain evaluated at analysis time points. LOCF was used to impute missing post-baseline values. |  |
| Subject analysis set title   | 8mg DA Assessment Wks 76 and 128                         |
| Subject analysis set type  | Sub-group analysis                                       |
| Subject analysis set description:<br>All participants who received study drug in Parts C and D and had physician's and participant's assessments of disease activity and pain evaluated at analysis time points. LOCF was used to impute missing post-baseline values. |  |
| Subject analysis set title   | 2mg LY3009104 PK Assessment for AUC Part A               |
| Subject analysis set type  | Sub-group analysis                                       |

Subject analysis set description:

All randomized participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 4mg LY3009104 PK Assessment for AUC Part A |
| Subject analysis set type  | Sub-group analysis                         |

Subject analysis set description:

All randomized participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 8mg LY3009104 PK Assessment for AUC Part A |
| Subject analysis set type  | Sub-group analysis                         |

Subject analysis set description:

All randomized participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 4mg Percentage Participants Meeting Low DA Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis  |

Subject analysis set description:

All participants who received study drug in Parts C and D and had DAS28-CRP evaluated at analysis time points.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 4-8mg Percentage Participants Meeting Low DA Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis  |

Subject analysis set description:

All participants who received study drug in Parts C and D and had DAS28-CRP evaluated at analysis time points.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 8mg Percentage Participants Meeting Low DA Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis  |

Subject analysis set description:

All participants who received study drug in Parts C and D and had DAS28-CRP evaluated at analysis time points.

|                            |                                     |
|----------------------------|-------------------------------------|
| Subject analysis set title | 4mg EULAR28 Response Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis                  |

Subject analysis set description:

All participants who received study drug in Parts C and D and had EULAR28 evaluated at analysis time points. LOCF was used to impute missing post-baseline values.

|                            |                                       |
|----------------------------|---------------------------------------|
| Subject analysis set title | 4-8mg EULAR28 Response Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis                    |

Subject analysis set description:

All participants who received study drug in Parts C and D and had EULAR28 evaluated at analysis time points. LOCF was used to impute missing post-baseline values.

|                            |                                     |
|----------------------------|-------------------------------------|
| Subject analysis set title | 8mg EULAR28 Response Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis                  |

Subject analysis set description:

All participants who received study drug in Parts C and D and had EULAR28 evaluated at analysis time points. LOCF was used to impute missing post-baseline values.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 4mg Mean Change ESR From Baseline To Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis                                  |

Subject analysis set description:

All participants who received study drug in Parts C and D and had ESR evaluated at analysis time points. LOCF was used to impute missing post-baseline values.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 4-8mg Mean Change ESR From Baseline To Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis                                    |

Subject analysis set description:

All participants who received study drug in Parts C and D and had ESR evaluated at analysis time points. LOCF was used to impute missing post-baseline values.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 8mg Mean Change ESR From Baseline To Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis                                  |

Subject analysis set description:

All participants who received study drug in Parts C and D and had ESR evaluated at analysis time points. LOCF was used to impute missing post-baseline values.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 2mg LY3009104 PK Assessment for Cmax Part A |
| Subject analysis set type  | Sub-group analysis                          |

Subject analysis set description:

All randomized participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 4mg LY3009104 PK Assessment for Cmax Part A |
| Subject analysis set type  | Sub-group analysis                          |

Subject analysis set description:

All randomized participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 8mg LY3009104 PK Assessment for Cmax Part A |
| Subject analysis set type  | Sub-group analysis                          |

Subject analysis set description:

All randomized participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 4mg Mean Change DAS28-CRP From Baseline To Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis  |

Subject analysis set description:

All participants who received study drug in Parts C and D and had DAS28-CRP evaluated at analysis time points. LOCF was used to impute missing post-baseline values.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 4-8mg Mean Change DAS28-CRP From Baseline To Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis  |

Subject analysis set description:

All participants who received study drug in Parts C and D and had DAS28-CRP evaluated at analysis time points. LOCF was used to impute missing post-baseline values.

|                            |   |
|----------------------------|---|
| Subject analysis set title | 8mg Mean Change DAS28-CRP From Baseline To Wks 76 and 128 |
| Subject analysis set type  | Sub-group analysis  |

Subject analysis set description:

All participants who received study drug in Parts C and D and had DAS28-CRP evaluated at analysis time points. LOCF was used to impute missing post-baseline values.

### **Primary: Percentage of Participants in the 4 mg and 8 mg Dose Groups Who Achieved an American College of Rheumatology 20 (ACR20) Responder Index Response Baseline through Week 12**

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants in the 4 mg and 8 mg Dose Groups Who Achieved an American College of Rheumatology 20 (ACR20) Responder Index Response Baseline through Week 12 <sup>[1]</sup> |
|-----------------|--|

End point description:

ACR20 Responder Index is a composite of clinical, laboratory, and functional measures in rheumatoid arthritis (RA). An ACR20 Responder is a participant who had  $\geq 20\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 20\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, Health Assessment Questionnaire-Disability Index (HAQ-DI) (assessment of participant's physical function), pain due to RA, and hsCRP. Participants who discontinue before analysis time point are treated as non-responders. Percentage of participants achieving ACR20 response = (number of ACR20 responders) / (number of participants analyzed) \* 100.

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

End point timeframe:

Baseline through Week 12

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: All randomized participants who received placebo, 4 mg or 8 mg LY3009104 in Part A. Participants for the 4mg and 8mg reporting groups were combined and number of participants analyzed is 102. Participants who had missing components of the ACR20 index at Week 12 had these components imputed by last observation carried forward (LOCF).

| End point values                  | Placebo QD - Part A | Combined 4mg and 8mg ACR20 Response Week 12 |  |  |
|-----------------------------------|---------------------|---|--|--|
| Subject group type                | Reporting group     | Subject analysis set                        |  |  |
| Number of subjects analysed       | 98                  | 102   |  |  |
| Units: percentage of participants |                     |   |  |  |
| number (not applicable)           | 41                  | 76  |  |  |

### Statistical analyses

|   |   |
|---|---|
| Statistical analysis title              | Statistical Analysis for Primary Endpoint                         |
| Comparison groups                       | Placebo QD - Part A v Combined 4mg and 8mg ACR20 Response Week 12 |
| Number of subjects included in analysis | 200   |
| Analysis specification                  | Pre-specified   |
| Analysis type                           | superiority   |
| P-value                                 | < 0.001 [2]   |
| Method                                  | Regression, Logistic  |

Notes:

[2] - A priori p-value significance threshold: 1-sided  $\leq 0.10$

### Secondary: Percentage of Participants Who Achieved an ACR20 Responder Index Response Baseline through Week 12 - Model Based Dose Response

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved an ACR20 Responder Index Response Baseline through Week 12 - Model Based Dose Response |
|-----------------|--|

End point description:

ACR20 Responder Index is a composite of clinical, laboratory, and functional measures in RA. An ACR20 Responder is a participant who had  $\geq 20\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 20\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, HAQ-DI (assessment of participant's physical function), pain due to RA, and hsCRP. Participants who discontinue before analysis time point are treated as non-responders. Percentage of participants achieving ACR20 response = (number of ACR20 responders) / (number of participants analyzed) \* 100. Data presented are model-based Bayesian posterior mean response rates with 95% credible interval.

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

End point timeframe:

Baseline through Week 12

| End point values                  | 1 milligram (mg)<br>LY3009104 QD<br>- Part A | 2 mg<br>LY3009104 QD<br>- Parts A and B | 4 mg<br>LY3009104 QD<br>- Parts A and B | 8 mg<br>LY3009104 QD<br>- Parts A and B |
|-----------------------------------|--|---|---|---|
| Subject group type                | Reporting group                              | Reporting group                         | Reporting group                         | Reporting group                         |
| Number of subjects analysed       | 49   | 52                                      | 52                                      | 50                                      |
| Units: percentage of participants |  |   |   |   |
| number (confidence interval 95%)  | 54.6 (42.2 to 67.1)                          | 55.2 (42.3 to 67.6)                     | 74.3 (63.1 to 84.1)                     | 77.2 (65.9 to 86.7)                     |

| End point values                  | Placebo QD -<br>Part A |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 98                     |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 42.1 (32.9 to 51.6)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Who Achieved an ACR20 Responder Index Response Baseline through Week 24

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved an ACR20 Responder Index Response Baseline through Week 24 |
|-----------------|--|

End point description:

ACR20 Responder Index is a composite of clinical, laboratory, and functional measures in RA. An ACR20 Responder is a participant who had  $\geq 20\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 20\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, HAQ-DI (assessment of participant's physical function), pain due to RA, and hsCRP. Participants who discontinue before analysis time points are treated as non-responders. Percentage of participants achieving ACR20 response = (number of ACR20 responders) / (number of participants treated) \* 100.

Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated. 9999=Data Not Available (N/A).

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

End point timeframe:

Baseline through Weeks 2, 4, 8, 12, 16, 20, 24

| End point values                  | 1 milligram (mg)<br>LY3009104 QD<br>- Part A | 2 mg<br>LY3009104 QD<br>- Parts A and B | 4 mg<br>LY3009104 QD<br>- Parts A and B | 8 mg<br>LY3009104 QD<br>- Parts A and B |
|-----------------------------------|--|---|---|---|
| Subject group type                | Reporting group                              | Reporting group                         | Reporting group                         | Reporting group                         |
| Number of subjects analysed       | 49 <sup>[3]</sup>                            | 52                                      | 52                                      | 50                                      |
| Units: percentage of participants |  |   |   |   |
| number (not applicable)           |  |   |   |   |

|         |      |    |    |    |
|---------|------|----|----|----|
| Week 2  | 29   | 21 | 42 | 44 |
| Week 4  | 43   | 37 | 60 | 54 |
| Week 8  | 43   | 42 | 67 | 72 |
| Week 12 | 57   | 54 | 75 | 78 |
| Week 16 | 9999 | 63 | 67 | 64 |
| Week 20 | 9999 | 71 | 77 | 78 |
| Week 24 | 9999 | 62 | 75 | 72 |

Notes:

[3] - Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated.

| End point values                  | Placebo QD - Part A |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 98 <sup>[4]</sup>   |  |  |  |
| Units: percentage of participants |                     |  |  |  |
| number (not applicable)           |                     |  |  |  |
| Week 2                            | 11                  |  |  |  |
| Week 4                            | 24                  |  |  |  |
| Week 8                            | 36                  |  |  |  |
| Week 12                           | 41                  |  |  |  |
| Week 16                           | 9999                |  |  |  |
| Week 20                           | 9999                |  |  |  |
| Week 24                           | 9999                |  |  |  |

Notes:

[4] - Participants were not dosed with placebo after Week 12; percentage was not calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Who Achieved an ACR20 Response Baseline through Weeks 76 and 128

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Who Achieved an ACR20 Response Baseline through Weeks 76 and 128 |
|-----------------|---|

End point description:

ACR20 Responder Index is a composite of clinical, laboratory, and functional measures in RA. An ACR20 Responder is a participant who had  $\geq 20\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 20\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, HAQ-DI (assessment of participant's physical function), pain due to RA, and hsCRP. Participants who discontinue before analysis time points are treated as non-responders. Percentage of participants achieving ACR20 response = (number of ACR20 responders) / (number of participants analyzed) \* 100.

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

End point timeframe:

Baseline through Weeks 76 and 128

| End point values                  | 4mg ACR20 Response Weeks (Wks) 76 and 128 | 4-8mg ACR20 Response Wks 76 and 128 | 8mg ACR20 Response Wks 76 and 128 |  |
|-----------------------------------|---|-------------------------------------|-----------------------------------|--|
| Subject group type                | Subject analysis set                      | Subject analysis set                | Subject analysis set              |  |
| Number of subjects analysed       | 108                                       | 61                                  | 32                                |  |
| Units: percentage of participants |   |                                     |                                   |  |
| number (not applicable)           |   |                                     |                                   |  |
| Week 76 (n=108, 61, 32)           | 71  | 67                                  | 59                                |  |
| Week 128 (n=79, 47, 18)           | 77  | 57                                  | 72                                |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Who Achieved an ACR 50 Responder Index Response Baseline through Week 24

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Who Achieved an ACR 50 Responder Index Response Baseline through Week 24 |
|-----------------|---|

End point description:

ACR50 Responder Index is a composite of clinical, laboratory, and functional measures in RA. An ACR50 Responder is a participant who had  $\geq 50\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 50\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, HAQ-DI (assessment of participant's physical function), pain due to RA, and hsCRP. Participants who discontinue before analysis time points are treated as non-responders. Percentage of participants achieving ACR50 response = (number of ACR50 responders) / (number of participants analyzed) \* 100.

Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated. 9999=Data Not Available (N/A).

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

End point timeframe:

Baseline through Weeks 2, 4, 8, 12, 16, 20, 24

| End point values                  | 1 milligram (mg) LY3009104 QD - Part A | 2 mg LY3009104 QD - Parts A and B | 4 mg LY3009104 QD - Parts A and B | 8 mg LY3009104 QD - Parts A and B |
|-----------------------------------|--|-----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type                | Reporting group                        | Reporting group                   | Reporting group                   | Reporting group                   |
| Number of subjects analysed       | 49 <sup>[5]</sup>                      | 52                                | 52                                | 50                                |
| Units: percentage of participants |  |                                   |                                   |                                   |
| number (not applicable)           |  |                                   |                                   |                                   |
| Week 2                            | 0                                      | 4                                 | 21                                | 4                                 |
| Week 4                            | 10                                     | 10                                | 29                                | 22                                |
| Week 8                            | 16                                     | 10                                | 33                                | 36                                |
| Week 12                           | 31                                     | 17                                | 35                                | 40                                |
| Week 16                           | 9999                                   | 19                                | 38                                | 44                                |
| Week 20                           | 9999                                   | 27                                | 46                                | 48                                |
| Week 24                           | 9999                                   | 19                                | 46                                | 54                                |



Notes:

[5] - Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated.

| End point values                  | Placebo QD - Part A |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 98 <sup>[6]</sup>   |  |  |  |
| Units: percentage of participants |                     |  |  |  |
| number (not applicable)           |                     |  |  |  |
| Week 2                            | 2                   |  |  |  |
| Week 4                            | 3                   |  |  |  |
| Week 8                            | 7                   |  |  |  |
| Week 12                           | 10                  |  |  |  |
| Week 16                           | 9999                |  |  |  |
| Week 20                           | 9999                |  |  |  |
| Week 24                           | 9999                |  |  |  |

Notes:

[6] - Participants were not dosed with Placebo LY3009104 after Week 12; percentage was not calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Who Achieved an ACR50 Response Baseline through Weeks 76 and 128

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Who Achieved an ACR50 Response Baseline through Weeks 76 and 128 |
|-----------------|---|

End point description:

ACR50 Responder Index is a composite of clinical, laboratory, and functional measures in RA. An ACR50 Responder is a participant who had  $\geq 50\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 50\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, HAQ-DI (assessment of participant's physical function), pain due to RA, and hsCRP. Participants who discontinue before analysis time points are treated as non-responders. Percentage of participants achieving ACR50 response = (number of ACR50 responders) / (number of participants analyzed) \* 100.

Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated.  
9999=Data Not Available (N/A).

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

End point timeframe:

Baseline through Weeks 76 and 128

| End point values                  | 4 mg LY3009104 QD - Parts C and D | 4 to 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D | 8 mg LY3009104 QD - Part C and 4 mg LY3009104 QD - Part D |  |
|-----------------------------------|-----------------------------------|--|---|--|
| Subject group type                | Reporting group                   | Reporting group  | Reporting group   |  |
| Number of subjects analysed       | 108                               | 61   | 32  |  |
| Units: percentage of participants |                                   |  |   |  |
| number (not applicable)           |                                   |  |   |  |
| Week 76 (n=108, 61, 32)           | 49                                | 41   | 44  |  |

|                         |    |    |    |  |
|-------------------------|----|----|----|--|
| Week 128 (n=79, 47, 18) | 58 | 30 | 44 |  |
|-------------------------|----|----|----|--|

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Who Achieved an ACR70 Responder Index Response Baseline through Week 24

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved an ACR70 Responder Index Response Baseline through Week 24 |
|-----------------|--|

End point description:

ACR70 Responder Index is a composite of clinical, laboratory, and functional measures in RA. An ACR70 Responder is a participant who had  $\geq 70\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 70\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, HAQ-DI (assessment of participant's physical function), pain due to RA, and hsCRP. Participants who discontinue before analysis time points are treated as non-responders. Percentage of participants achieving ACR70 response = (number of ACR70 responders) / (number of participants analyzed) \* 100.

Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated. 9999=Data Not Available (N/A).

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

End point timeframe:

Baseline through Weeks 2, 4, 8, 12, 16, 20, 24

| End point values   | 1 milligram (mg)<br>LY3009104 QD<br>- Part A | 2 mg<br>LY3009104 QD<br>- Parts A and B | 4 mg<br>LY3009104 QD<br>- Parts A and B | 8 mg<br>LY3009104 QD<br>- Parts A and B |
|--|--|---|---|---|
| Subject group type   | Reporting group                              | Reporting group                         | Reporting group                         | Reporting group                         |
| Number of subjects analysed                                  | 49 <sup>[7]</sup>                            | 52                                      | 52                                      | 50                                      |
| Units: percentage of participants<br>number (not applicable) |  |   |   |   |
| Week 2   | 0  | 2                                       | 12                                      | 0                                       |
| Week 4   | 2  | 4                                       | 10                                      | 6                                       |
| Week 8   | 4  | 4                                       | 15                                      | 22                                      |
| Week 12  | 12   | 8                                       | 23                                      | 20                                      |
| Week 16  | 9999   | 8                                       | 23                                      | 30                                      |
| Week 20  | 9999   | 10                                      | 21                                      | 26                                      |
| Week 24  | 9999   | 10                                      | 27                                      | 24                                      |

Notes:

[7] - Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated.

| End point values                  | Placebo QD -<br>Part A |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 98 <sup>[8]</sup>      |  |  |  |
| Units: percentage of participants |                        |  |  |  |

|                         |      |  |  |  |
|-------------------------|------|--|--|--|
| number (not applicable) |      |  |  |  |
| Week 2                  | 0    |  |  |  |
| Week 4                  | 0    |  |  |  |
| Week 8                  | 0    |  |  |  |
| Week 12                 | 2    |  |  |  |
| Week 16                 | 9999 |  |  |  |
| Week 20                 | 9999 |  |  |  |
| Week 24                 | 9999 |  |  |  |

Notes:

[8] - Participants were not dosed with placebo after Week 12; percentage was not calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Who Achieved an ACR70 Response Baseline through Weeks 76 and 128

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Who Achieved an ACR70 Response Baseline through Weeks 76 and 128 |
|-----------------|---|

End point description:

ACR70 Responder Index is a composite of clinical, laboratory, and functional measures in RA. An ACR70 Responder is a participant who had  $\geq 70\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 70\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, HAQ-DI (assessment of participant's physical function), pain due to RA, and hsCRP. Participants who discontinue before analysis time points are treated as non-responders. Percentage of participants achieving ACR70 response = (number of ACR70 responders) / (number of participants analyzed) \* 100.

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

End point timeframe:

Baseline through Weeks 76 and 128

| End point values                  | 4mg ACR70 Response Wks 76 and 128 | 4-8mg ACR70 Response Wks 76 and 128 | 8mg ACR70 Response Wks 76 and 128 |  |
|-----------------------------------|-----------------------------------|-------------------------------------|-----------------------------------|--|
| Subject group type                | Subject analysis set              | Subject analysis set                | Subject analysis set              |  |
| Number of subjects analysed       | 108                               | 61                                  | 32                                |  |
| Units: percentage of participants |                                   |                                     |                                   |  |
| number (not applicable)           |                                   |                                     |                                   |  |
| Week 76 (n=108, 61, 32)           | 29                                | 18                                  | 25                                |  |
| Week 128 (n=79, 47, 18)           | 28                                | 17                                  | 22                                |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Who Achieved an ACR50 Response Baseline through Week 12 - Model Based Dose Response

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Who Achieved an ACR50 Response Baseline through Week 12 - Model Based Dose Response |
|-----------------|--|

**End point description:**

ACR50 Responder Index is a composite of clinical, laboratory, and functional measures in RA. An ACR50 Responder is a participant who had  $\geq 50\%$  improvement from baseline in both 68 tender and 66 swollen joint counts and  $\geq 50\%$  improvement in at least 3 of 5 criteria: Patient's and Physician's Global Assessment of Disease Activity, HAQ-DI (assessment of participant's physical function), pain due to RA, and hsCRP. Participants who discontinue before analysis time point are treated as non-responders. Percentage of participants achieving ACR50 response = (number of ACR50 responders) / (number of participants analyzed) \* 100. Data presented are model-based Bayesian posterior mean response rates with 95% credible interval.

|                          |           |
|--------------------------|-----------|
| End point type           | Secondary |
| End point timeframe:     |           |
| Baseline through Week 12 |           |

| End point values                  | 1 milligram (mg) LY3009104 QD - Part A | 2 mg LY3009104 QD - Parts A and B | 4 mg LY3009104 QD - Parts A and B | 8 mg LY3009104 QD - Parts A and B |
|-----------------------------------|--|-----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type                | Reporting group                        | Reporting group                   | Reporting group                   | Reporting group                   |
| Number of subjects analysed       | 49                                     | 52                                | 52                                | 50                                |
| Units: percentage of participants |  |                                   |                                   |                                   |
| number (confidence interval 95%)  | 26.5 (16 to 39.2)                      | 18.8 (9.9 to 29.7)                | 34.4 (23.1 to 46.7)               | 39.2 (27.1 to 52.2)               |

| End point values                  | Placebo QD - Part A |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 98                  |  |  |  |
| Units: percentage of participants |                     |  |  |  |
| number (confidence interval 95%)  | 12 (6.5 to 18.8)    |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: ACR Percent Improvement (ACR-N)**

|                 |                                 |
|-----------------|---------------------------------|
| End point title | ACR Percent Improvement (ACR-N) |
|-----------------|---------------------------------|

**End point description:**

ACR-N is a continuous measure of clinical, laboratory, and functional outcomes in RA that characterizes percentage (%) of improvement in disease activity from baseline based on ACR core set. This index was calculated as minimum of a) % of improvement in TJC, b) % of improvement in SJC, and c) third highest percentage of improvement of remaining 5 ACR core criteria: If  $\geq 3$  components of the 5 ACR core criteria were missing, then c) was set to missing; if any of 3 components a), b), or c) were missing, then ACR-N was set to missing. Percentage of improvement was truncated to a range of -100 to 100 to minimize impact of outliers (greater scores indicate greater % improvement) and negative scores indicate a decline. Data presented are model-based Bayesian posterior mean response rates with 95% credible interval.

|                          |           |
|--------------------------|-----------|
| End point type           | Secondary |
| End point timeframe:     |           |
| Baseline through Week 12 |           |

| <b>End point values</b>          | 1 milligram (mg)<br>LY3009104 QD<br>- Part A | 2 mg<br>LY3009104 QD<br>- Parts A and B | 4 mg<br>LY3009104 QD<br>- Parts A and B | 8 mg<br>LY3009104 QD<br>- Parts A and B |
|----------------------------------|--|---|---|---|
| Subject group type               | Reporting group                              | Reporting group                         | Reporting group                         | Reporting group                         |
| Number of subjects analysed      | 49   | 52                                      | 52                                      | 50                                      |
| Units: percentage of improvement |  |   |   |   |
| number (confidence interval 95%) | 17.3 (7.57 to 28.22)                         | 19.42 (8.74 to 29.25)                   | 28.59 (17.67 to 40.83)                  | 29 (17.67 to 41.47)                     |

| <b>End point values</b>          | Placebo QD -<br>Part A |  |  |  |
|----------------------------------|------------------------|--|--|--|
| Subject group type               | Reporting group        |  |  |  |
| Number of subjects analysed      | 98                     |  |  |  |
| Units: percentage of improvement |                        |  |  |  |
| number (confidence interval 95%) | 10.97 (-0.39 to 21.64) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change from Baseline to Weeks 12 and 24 in Tender and Swollen Joint Counts (TJC and SJC)

|                 |   |
|-----------------|---|
| End point title | Mean Change from Baseline to Weeks 12 and 24 in Tender and Swollen Joint Counts (TJC and SJC) |
|-----------------|---|

End point description:

TJC is the number of tender and painful joints determined for each participant by examination of 68 joints. Joints were assessed by pressure and joint manipulation on physical examination. Participants were asked for pain sensations on these manipulations and watched for spontaneous pain reactions. Any positive response on pressure, movement, or both was translated into a single tender-versus-nontender dichotomy. SJC is the number of swollen joints determined for each participant by examination of 66 joints. Joints were classified as either swollen or not swollen. Swelling was defined as palpable fluctuating synovitis of the joint.

Participants were not dosed with 1 mg LY3009104 after Week 12; mean and standard deviation (SD) were not calculated.

9999=Data Not Available (N/A).

All randomized participants who received study drug in Parts A and B and had TJC and SJC evaluated at analysis time points. LOCF was used to impute missing post-baseline values

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

End point timeframe:

Baseline, Weeks 12 and 24

| End point values                     | 1 milligram (mg)<br>LY3009104 QD<br>- Part A | 2 mg<br>LY3009104 QD<br>- Parts A and B | 4 mg<br>LY3009104 QD<br>- Parts A and B | 8 mg<br>LY3009104 QD<br>- Parts A and B |
|--------------------------------------|--|---|---|---|
| Subject group type                   | Reporting group                              | Reporting group                         | Reporting group                         | Reporting group                         |
| Number of subjects analysed          | 49 <sup>[9]</sup>                            | 52                                      | 51                                      | 50                                      |
| Units: number of joints              |  |   |   |   |
| arithmetic mean (standard deviation) |  |   |   |   |
| TJC - Week 12                        | -8.4 (± 12.7)                                | -11.3 (± 13.5)                          | -12.2 (± 10.45)                         | -14.7 (± 12.97)                         |
| TJC - Week 24                        | 9999 (± 9999)                                | -12.4 (± 12.6)                          | -14 (± 9.54)                            | -17.5 (± 11.23)                         |
| SJC - Week 12                        | -8.1 (± 7.24)                                | -8.9 (± 9.03)                           | -9.6 (± 6.49)                           | -10.4 (± 8.88)                          |
| SJC - Week 24                        | 9999 (± 9999)                                | -10 (± 8.16)                            | -10.5 (± 6.42)                          | -12.2 (± 7.29)                          |

Notes:

[9] - Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated.

| End point values                     | Placebo QD -<br>Part A |  |  |  |
|--------------------------------------|------------------------|--|--|--|
| Subject group type                   | Reporting group        |  |  |  |
| Number of subjects analysed          | 98 <sup>[10]</sup>     |  |  |  |
| Units: number of joints              |                        |  |  |  |
| arithmetic mean (standard deviation) |                        |  |  |  |
| TJC - Week 12                        | -7.6 (± 12.31)         |  |  |  |
| TJC - Week 24                        | 9999 (± 9999)          |  |  |  |
| SJC - Week 12                        | -6.7 (± 7.97)          |  |  |  |
| SJC - Week 24                        | 9999 (± 9999)          |  |  |  |

Notes:

[10] - Participants were not dosed with placebo after Week 12; mean and SD were not calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline to Weeks 76 and 128 in TJC and SJC

|   |  |
|---|--|
| End point title   | Mean Change from Baseline to Weeks 76 and 128 in TJC and SJC |
| End point description:  |  |
| TJC is the number of tender and painful joints determined for each participant by examination of 68 joints. Joints were assessed by pressure and joint manipulation on physical examination. Participants were asked for pain sensations on these manipulations and watched for spontaneous pain reactions. Any positive response on pressure, movement, or both was translated into a single tender-versus-nontender dichotomy. SJC is the number of swollen joints determined for each participant by examination of 66 joints. Joints were classified as either swollen or not swollen. Swelling was defined as palpable fluctuating synovitis of the joint. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Baseline, Weeks 76 and 128  |  |

| End point values                     | 4mg Mean Change TJC and SJC From Baseline To Wks 76 and 128 | 4-8mg Mean Change TJC and SJC From Baseline To Wks 76 and 128 | 8mg Mean Change TJC and SJC From Baseline To Wks 76 and 128 |  |
|--------------------------------------|---|---|---|--|
| Subject group type                   | Subject analysis set  | Subject analysis set  | Subject analysis set  |  |
| Number of subjects analysed          | 108   | 61  | 32  |  |
| Units: units on a scale              |   |   |   |  |
| arithmetic mean (standard deviation) |   |   |   |  |
| TJC - Week 76 (n=108, 61, 32)        | -15.7 (± 11.26)   | -16 (± 13.37)   | -18.1 (± 12.06)   |  |
| TJC - Week 128 (n=79, 47, 18)        | -16.4 (± 11.01)   | -15.3 (± 12.56)   | -14 (± 13.68)   |  |
| SJC - Week 76 (n=108, 61, 32)        | -11.6 (± 6.4)   | -12.9 (± 7.8)   | -12.4 (± 7.67)  |  |
| SJC - Week 128 (n=79, 47, 18)        | -11.4 (± 6.81)  | -12.4 (± 8.01)  | -11.6 (± 6.23)  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline to Weeks 12 and 24 in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score

|                 |   |
|-----------------|---|
| End point title | Mean Change from Baseline to Weeks 12 and 24 in Health Assessment Questionnaire-Disability Index (HAQ-DI) Score |
|-----------------|---|

End point description:

The HAQ-DI questionnaire assesses the participant's self-perception on the degree of difficulty [0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty), and 3 (unable to do)] when dressing and grooming, arising, eating, walking, hygiene, reaching, gripping, and performing other daily activities. Scores for each functional area were averaged to calculate HAQ-DI scores, which ranged from 0 (no disability) to 3 (worst disability). A decrease in HAQ-DI score indicated an improvement in the participant's condition.

Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated. 9999=Data Not Available (N/A).

|                           |           |
|---------------------------|-----------|
| End point type            | Secondary |
| End point timeframe:      |           |
| Baseline, Weeks 12 and 24 |           |

| End point values                     | 1 milligram (mg) LY3009104 QD - Part A | 2 mg LY3009104 QD - Parts A and B | 4 mg LY3009104 QD - Parts A and B | 8 mg LY3009104 QD - Parts A and B |
|--------------------------------------|--|-----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type                   | Reporting group                        | Reporting group                   | Reporting group                   | Reporting group                   |
| Number of subjects analysed          | 49 <sup>[11]</sup>                     | 52                                | 51 <sup>[12]</sup>                | 50                                |
| Units: units on a scale              |  |                                   |                                   |                                   |
| arithmetic mean (standard deviation) |  |                                   |                                   |                                   |
| Week 12                              | -0.35 (± 0.528)                        | -0.18 (± 0.524)                   | -0.33 (± 0.459)                   | -0.39 (± 0.497)                   |
| Week 24                              | 9999 (± 9999)                          | -0.18 (± 0.505)                   | -0.32 (± 0.506)                   | -0.44 (± 0.529)                   |

Notes:

[11] - Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated.

[12] - Participants who received study drug in Parts A and B and had evaluable HAQ-DI data.

|                                      |                     |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| <b>End point values</b>              | Placebo QD - Part A |  |  |  |
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 98 <sup>[13]</sup>  |  |  |  |
| Units: units on a scale              |                     |  |  |  |
| arithmetic mean (standard deviation) |                     |  |  |  |
| Week 12                              | -0.1 (± 0.406)      |  |  |  |
| Week 24                              | 9999 (± 9999)       |  |  |  |

Notes:

[13] - Participants were not dosed with placebo after Week 12; mean and SD were not calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline to Weeks 76 and 128 in HAQ-DI Score

|                 |   |
|-----------------|---|
| End point title | Mean Change from Baseline to Weeks 76 and 128 in HAQ-DI Score |
|-----------------|---|

End point description:

The HAQ-DI questionnaire assesses the participant's self-perception on the degree of difficulty [0 (without any difficulty), 1 (with some difficulty), 2 (with much difficulty), and 3 (unable to do)] when dressing and grooming, arising, eating, walking, hygiene, reaching, gripping, and performing other daily activities. Scores for each functional area were averaged to calculate HAQ-DI scores, which ranged from 0 (no disability) to 3 (worst disability). A decrease in HAQ-DI score indicated an improvement in the participant's condition.

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

End point timeframe:

Baseline, Weeks 76 and 128

|                                      |  |  |  |  |
|--------------------------------------|--|--|--|--|
| <b>End point values</b>              | 4mg Mean Change HAQ-DI From Baseline To Wks 76 and 128 | 4-8mg Mean Change HAQ-DI From Baseline To Wks 76 and 128 | 8mg Mean Change HAQ-DI From Baseline To Wks 76 and 128 |  |
| Subject group type                   | Subject analysis set                                   | Subject analysis set                                     | Subject analysis set                                   |  |
| Number of subjects analysed          | 108  | 61   | 32   |  |
| Units: units on a scale              |  |  |  |  |
| arithmetic mean (standard deviation) |  |  |  |  |
| Week 76 (n=108, 61, 32)              | -0.34 (± 0.58)   | -0.29 (± 0.53)   | -0.55 (± 0.58)   |  |
| Week 128 (n=79, 47, 18)              | -0.31 (± 0.61)   | -0.22 (± 0.56)   | -0.3 (± 0.66)  |  |

## Statistical analyses



**Secondary: Mean Change from Baseline to Weeks 12 and 24 in High-Sensitivity C-Reactive Protein (hsCRP)**

|                 |   |
|-----------------|---|
| End point title | Mean Change from Baseline to Weeks 12 and 24 in High-Sensitivity C-Reactive Protein (hsCRP) |
|-----------------|---|

## End point description:

hsCRP is a laboratory analyte that is an indicator of inflammation. Decreases in hsCRP represent reductions in inflammation.

Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated. 9999=Data Not Available (N/A).

|                           |           |
|---------------------------|-----------|
| End point type            | Secondary |
| End point timeframe:      |           |
| Baseline, Weeks 12 and 24 |           |

| End point values                     | 1 milligram (mg)<br>LY3009104 QD<br>- Part A | 2 mg<br>LY3009104 QD<br>- Parts A and B | 4 mg<br>LY3009104 QD<br>- Parts A and B | 8 mg<br>LY3009104 QD<br>- Parts A and B |
|--------------------------------------|--|---|---|---|
| Subject group type                   | Reporting group                              | Reporting group                         | Reporting group                         | Reporting group                         |
| Number of subjects analysed          | 49 <sup>[14]</sup>                           | 52                                      | 51 <sup>[15]</sup>                      | 50                                      |
| Units: mg/L                          |  |   |   |   |
| arithmetic mean (standard deviation) |  |   |   |   |
| Week 12                              | -6.14 (± 10.236)                             | -3.39 (± 19.409)                        | -7.06 (± 16.945)                        | -2.32 (± 32.582)                        |
| Week 24                              | 9999 (± 9999)                                | -4.76 (± 19.819)                        | -4.95 (± 19.819)                        | -7.61 (± 17.548)                        |

## Notes:

[14] - Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated.

[15] - Participants who received study drug in Parts A and B and had evaluable hsCRP data.

| End point values                     | Placebo QD -<br>Part A |  |  |  |
|--------------------------------------|------------------------|--|--|--|
| Subject group type                   | Reporting group        |  |  |  |
| Number of subjects analysed          | 97 <sup>[16]</sup>     |  |  |  |
| Units: mg/L                          |                        |  |  |  |
| arithmetic mean (standard deviation) |                        |  |  |  |
| Week 12                              | 1.5 (± 34.107)         |  |  |  |
| Week 24                              | 9999 (± 9999)          |  |  |  |

## Notes:

[16] - Participants were not dosed with placebo after Week 12, therefore mean and SD were not calculated.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Mean Change from Baseline to Weeks 76 and 128 in hsCRP**

|                 |  |
|-----------------|--|
| End point title | Mean Change from Baseline to Weeks 76 and 128 in hsCRP |
|-----------------|--|

End point description:

hsCRP is a laboratory analyte that is an indicator of inflammation. Decreases in hsCRP represent reductions in inflammation.

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

End point timeframe:

Baseline, Weeks 76 and 128

| End point values                     | 4mg Mean Change hsCRP From Baseline To Wks 76 and 128 | 4-8mg Mean Change hsCRP From Baseline To Wks 76 and 128 | 8mg Mean Change hsCRP From Baseline To Wks 76 and 128 |  |
|--------------------------------------|---|---|---|--|
| Subject group type                   | Subject analysis set                                  | Subject analysis set                                    | Subject analysis set                                  |  |
| Number of subjects analysed          | 108   | 61  | 32  |  |
| Units: mg/L                          |   |   |   |  |
| arithmetic mean (standard deviation) |   |   |   |  |
| Week 76 (n=108, 61, 32)              | -3.9 (± 22.43)  | -3.3 (± 14.28)  | -2.9 (± 25.36)  |  |
| Week 128 (n=79, 47, 18)              | -6.8 (± 13.66)  | -2.9 (± 21.88)  | -8.2 (± 12.33)  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline to Weeks 12 and 24 in Erythrocyte Sedimentation Rate (ESR)

|                 |  |
|-----------------|--|
| End point title | Mean Change from Baseline to Weeks 12 and 24 in Erythrocyte Sedimentation Rate (ESR) |
|-----------------|--|

End point description:

ESR is a laboratory analyte that is an indicator of inflammation. Decreases represent reductions in inflammation.

Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated. 9999=Data Not Available (N/A).

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

End point timeframe:

Baseline, Weeks 12 and 24

| End point values                     | 1 milligram (mg) LY3009104 QD - Part A | 2 mg LY3009104 QD - Parts A and B | 4 mg LY3009104 QD - Parts A and B | 8 mg LY3009104 QD - Parts A and B |
|--------------------------------------|--|-----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type                   | Reporting group                        | Reporting group                   | Reporting group                   | Reporting group                   |
| Number of subjects analysed          | 44 <sup>[17]</sup>                     | 51 <sup>[18]</sup>                | 50 <sup>[19]</sup>                | 49 <sup>[20]</sup>                |
| Units: mm/hr                         |  |                                   |                                   |                                   |
| arithmetic mean (standard deviation) |  |                                   |                                   |                                   |
| Week 12 (n=44, 51, 50, 49, 83)       | -11.6 (± 14.45)                        | -6.4 (± 16.81)                    | -11.5 (± 17.28)                   | 13.9 (± 22.42)                    |

|                              |               |                |             |                 |
|------------------------------|---------------|----------------|-------------|-----------------|
| Week 24 (n=0, 50, 48, 45, 0) | 9999 (± 9999) | -6.9 (± 13.89) | -9.2 (± 19) | -13.7 (± 21.62) |
|------------------------------|---------------|----------------|-------------|-----------------|

Notes:

[17] - Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated.

[18] - Participants who received study drug in Parts A and B and had evaluable ESR data.

[19] - Participants who received study drug in Parts A and B and had evaluable ESR data.

[20] - Participants who received study drug in Parts A and B and had evaluable ESR data.

|                                      |                     |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| <b>End point values</b>              | Placebo QD - Part A |  |  |  |
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 83 <sup>[21]</sup>  |  |  |  |
| Units: mm/hr                         |                     |  |  |  |
| arithmetic mean (standard deviation) |                     |  |  |  |
| Week 12 (n=44, 51, 50, 49, 83)       | -6 (± 19.49)        |  |  |  |
| Week 24 (n=0, 50, 48, 45, 0)         | 9999 (± 9999)       |  |  |  |

Notes:

[21] - Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline to Weeks 76 and 128 in ESR

|   |  |
|---|--|
| End point title   | Mean Change from Baseline to Weeks 76 and 128 in ESR |
| End point description:  |  |
| ESR is a laboratory analyte that is an indicator of inflammation. Decreases represent reductions in inflammation. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Baseline, Weeks 76 and 128  |  |

|                                      |   |   |   |  |
|--------------------------------------|---|---|---|--|
| <b>End point values</b>              | 4mg Mean Change ESR From Baseline To Wks 76 and 128 | 4-8mg Mean Change ESR From Baseline To Wks 76 and 128 | 8mg Mean Change ESR From Baseline To Wks 76 and 128 |  |
| Subject group type                   | Subject analysis set                                | Subject analysis set                                  | Subject analysis set                                |  |
| Number of subjects analysed          | 108 <sup>[22]</sup>                                 | 61 <sup>[23]</sup>                                    | 32 <sup>[24]</sup>                                  |  |
| Units: mm/hr                         |   |   |   |  |
| arithmetic mean (standard deviation) |   |   |   |  |
| Week 76 (n=108, 61, 32)              | -13 (± 18.84)                                       | -7.4 (± 26.28)  | -8.9 (± 23.12)                                      |  |
| Week 128 (n=79, 47, 18)              | -16 (± 18.74)                                       | -8.5 (± 23.11)  | -15.5 (± 23.07)                                     |  |

Notes:

[22] - Participants who received study drug Parts C and D and had evaluable ESR data.

[23] - Participants who received study drug Parts C and D and had evaluable ESR data.

[24] - Participants who received study drug Parts C and D and had evaluable ESR data.

## Statistical analyses

**Secondary: Mean Change from Baseline to Weeks 12 and 24 in Physician's Global Assessment of Disease Activity, Patient's Global Assessment of Disease Activity and Patient's Assessment of Pain**

|                 |   |
|-----------------|---|
| End point title | Mean Change from Baseline to Weeks 12 and 24 in Physician's Global Assessment of Disease Activity, Patient's Global Assessment of Disease Activity and Patient's Assessment of Pain |
|-----------------|---|

## End point description:

Physician's and Patient's Assessments of Disease Activity (DA) assessed using a visual analog scale (VAS) that ranged from 0 to 100 millimeters (mm), where 0 indicated no arthritis activity and 100 indicated extremely active arthritis. Patient's assessment of pain due to arthritis was also assessed using a VAS that ranged from 0 (no pain) to 100 mm (worst possible pain).

Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated. 9999=Data Not Available (N/A).

|                           |           |
|---------------------------|-----------|
| End point type            | Secondary |
| End point timeframe:      |           |
| Baseline, Weeks 12 and 24 |           |

| End point values                       | 1 milligram (mg)<br>LY3009104 QD<br>- Part A | 2 mg<br>LY3009104 QD<br>- Parts A and B | 4 mg<br>LY3009104 QD<br>- Parts A and B | 8 mg<br>LY3009104 QD<br>- Parts A and B |
|--|--|---|---|---|
| Subject group type                     | Reporting group                              | Reporting group                         | Reporting group                         | Reporting group                         |
| Number of subjects analysed            | 49 <sup>[25]</sup>                           | 52                                      | 51 <sup>[26]</sup>                      | 50                                      |
| Units: units on a scale                |  |   |   |   |
| arithmetic mean (standard deviation)   |  |   |   |   |
| Physician's Assessment of DA - Week 12 | -23.9 (± 18.49)                              | -25 (± 20.81)                           | -30.4 (± 18.75)                         | -33.5 (± 19.49)                         |
| Physician's Assessment of DA - Week 24 | 9999 (± 9999)                                | -27.8 (± 21.13)                         | -35.5 (± 17.72)                         | -37.8 (± 18.73)                         |
| Patient's Assessment of DA - Week 12   | -24.9 (± 27.26)                              | -16.2 (± 22.43)                         | -25.4 (± 21.61)                         | -29.8 (± 21.2)                          |
| Patient's Assessment of DA - Week 24   | 9999 (± 9999)                                | -16.9 (± 24.96)                         | -30.2 (± 21.85)                         | -30 (± 20.9)                            |
| Patient's Assessment of Pain - Week 12 | -22.8 (± 27.39)                              | -14.2 (± 17.82)                         | -25 (± 19.22)                           | -25.3 (± 20.31)                         |
| Patient's Assessment of Pain - Week 24 | 9999 (± 9999)                                | -14.7 (± 20.57)                         | -27.3 (± 22.11)                         | -26.9 (± 19.22)                         |

## Notes:

[25] - Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated.

[26] - Participants who received study drug in Parts A and B and had evaluable DA assessment data,

| End point values                       | Placebo QD -<br>Part A |  |  |  |
|--|------------------------|--|--|--|
| Subject group type                     | Reporting group        |  |  |  |
| Number of subjects analysed            | 98 <sup>[27]</sup>     |  |  |  |
| Units: units on a scale                |                        |  |  |  |
| arithmetic mean (standard deviation)   |                        |  |  |  |
| Physician's Assessment of DA - Week 12 | -19 (± 21.4)           |  |  |  |
| Physician's Assessment of DA - Week 24 | 9999 (± 9999)          |  |  |  |

|  |                      |  |  |  |
|--|----------------------|--|--|--|
| Patient's Assessment of DA - Week 12   | -10.3 ( $\pm$ 22.02) |  |  |  |
| Patient's Assessment of DA - Week 24   | 9999 ( $\pm$ 9999)   |  |  |  |
| Patient's Assessment of Pain - Week 12 | -8.8 ( $\pm$ 22.77)  |  |  |  |
| Patient's Assessment of Pain - Week 24 | 9999 ( $\pm$ 9999)   |  |  |  |

Notes:

[27] - Participants were not dosed with placebo after Week 12; mean and SD were not calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline to Weeks 76 and 128 in Physician's Global Assessment of Disease Activity, Patient's Global Assessment of Disease Activity and Patient's Assessment of Pain

|                 |  |
|-----------------|--|
| End point title | Mean Change from Baseline to Weeks 76 and 128 in Physician's Global Assessment of Disease Activity, Patient's Global Assessment of Disease Activity and Patient's Assessment of Pain |
|-----------------|--|

End point description:

Physician's and Patient's assessments of DA assessed using a VAS that ranged from 0 to 100 mm, where 0 indicated no arthritis activity and 100 indicated extremely active arthritis. Patient's assessment of pain due to arthritis assessed using a VAS that ranged from 0 (no pain) to 100 mm (worst possible pain).

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

End point timeframe:

Baseline, Weeks 76 and 128

| End point values                                   | 4mg DA Assessment Wks 76 and 128 | 4-8mg DA Assessment Wks 76 and 128 | 8mg DA Assessment Wks 76 and 128 |  |
|--|----------------------------------|------------------------------------|----------------------------------|--|
| Subject group type                                 | Subject analysis set             | Subject analysis set               | Subject analysis set             |  |
| Number of subjects analysed                        | 108                              | 61                                 | 32                               |  |
| Units: units on a scale                            |                                  |                                    |                                  |  |
| arithmetic mean (standard deviation)               |                                  |                                    |                                  |  |
| Physician Assessment of DA-Week 76 (n=108, 61, 32) | -40.3 ( $\pm$ 19.15)             | -32.3 ( $\pm$ 23.37)               | -40.5 ( $\pm$ 21.44)             |  |
| Physician Assessment of DA-Week 128 (n=79, 47, 18) | -39.5 ( $\pm$ 20.32)             | -31 ( $\pm$ 25.54)                 | -34 ( $\pm$ 27.51)               |  |
| Patient Assessment of DA-Week 76 (n=108, 61, 32)   | -27.5 ( $\pm$ 26.49)             | -27.5 ( $\pm$ 25.52)               | -27.6 ( $\pm$ 24.11)             |  |
| Patient Assessment of DA-Week 128 (n=79, 47, 18)   | -27.9 ( $\pm$ 27.4)              | -19.3 ( $\pm$ 29.72)               | -27.6 ( $\pm$ 25.17)             |  |
| Patient Assessment of Pain-Week 76 (n=108, 61, 32) | -25.1 ( $\pm$ 24.1)              | -27.3 ( $\pm$ 24.24)               | -23.4 ( $\pm$ 23.49)             |  |
| Patient Assessment of Pain-Week 128 (n=79, 47, 18) | -24.2 ( $\pm$ 24.35)             | -18 ( $\pm$ 28.85)                 | -22.3 ( $\pm$ 22.99)             |  |

## Statistical analyses

## Secondary: Mean Change from Baseline to Weeks 12 and 24 in Disease Activity Score (DAS) Based on the 28 Diarthrodial Joint Count and CRP Level (DAS28-CRP)

|                 |   |
|-----------------|---|
| End point title | Mean Change from Baseline to Weeks 12 and 24 in Disease Activity Score (DAS) Based on the 28 Diarthrodial Joint Count and CRP Level (DAS28-CRP) |
|-----------------|---|

### End point description:

Disease Activity Score (DAS) modified to include 28 joint count (DAS28) consisted of composite score of following variables: tender joint count-28 (TJC28), swollen joint count-28 (SJC28), CRP (mg/L), and Patient's Global Assessment of Disease Activity using VAS (patient's global VAS).  $DAS28-CRP = 0.56 \times \sqrt{TJC28} + 0.28 \times \sqrt{SJC28} + 0.36 \times \ln(CRP + 1) + 0.014 \times \text{patient's global VAS} + 0.96$ . Scores ranged from 1.0-9.4, where lower scores indicated less disease activity, and remission was  $DAS28-CRP < 2.6$ . A decrease in DAS28-CRP indicated an improvement in participant's condition.

Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated. 9999=Data Not Available (N/A).

|                      |                           |
|----------------------|---------------------------|
| End point type       | Secondary                 |
| End point timeframe: | Baseline, Weeks 12 and 24 |

| End point values                     | 1 milligram (mg) LY3009104 QD - Part A | 2 mg LY3009104 QD - Parts A and B | 4 mg LY3009104 QD - Parts A and B | 8 mg LY3009104 QD - Parts A and B |
|--------------------------------------|--|-----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type                   | Reporting group                        | Reporting group                   | Reporting group                   | Reporting group                   |
| Number of subjects analysed          | 49 <sup>[28]</sup>                     | 52                                | 50 <sup>[29]</sup>                | 50                                |
| Units: units on a scale              |  |                                   |                                   |                                   |
| arithmetic mean (standard deviation) |  |                                   |                                   |                                   |
| Week 12                              | -1.47 (± 1.299)                        | -1.4 (± 1.21)                     | -2.09 (± 1.22)                    | -2.15 (± 1.273)                   |
| Week 24                              | 9999 (± 9999)                          | -1.53 (± 1.187)                   | -2.25 (± 1.054)                   | -2.47 (± 1.28)                    |

### Notes:

[28] - Participants were not dosed with 1 mg LY3009104 after Week 12; mean and SD were not calculated.

[29] - Participants who received drug in Parts A and B and had evaluable DAS28-CRP data.

| End point values                     | Placebo QD - Part A |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 93 <sup>[30]</sup>  |  |  |  |
| Units: units on a scale              |                     |  |  |  |
| arithmetic mean (standard deviation) |                     |  |  |  |
| Week 12                              | -0.98 (± 1.141)     |  |  |  |
| Week 24                              | 9999 (± 9999)       |  |  |  |

### Notes:

[30] - Participants were not dosed with placebo after Week 12; mean and SD were not calculated.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change from Baseline to Weeks 76 and 128 in DAS28-CRP

|                 |  |
|-----------------|--|
| End point title | Mean Change from Baseline to Weeks 76 and 128 in DAS28-CRP |
|-----------------|--|

End point description:

Disease Activity Score (DAS) modified to include 28 joint count (DAS28) consisted of composite score of following variables: tender joint count (TJC28), swollen joint count (SJC28), CRP (mg/L), and Patient's Global Assessment of Disease Activity using visual analog scale (VAS) (patient's global VAS).  $DAS28-CRP = 0.56 * \sqrt{TJC28} + 0.28 * \sqrt{SJC28} + 0.36 * \ln(CRP + 1) + 0.014 * \text{patient's global VAS} + 0.96$ . Scores ranged from 1.0-9.4, where lower scores indicated less disease activity and remission is  $DAS28-CRP < 2.6$ . A decrease in DAS28-CRP indicated an improvement in participant's condition.

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

End point timeframe:

Baseline, Weeks 76 and 128

| End point values                     | 4mg Mean Change DAS28-CRP From Baseline To Wks 76 and 128 | 4-8mg Mean Change DAS28-CRP From Baseline To Wks 76 and 128 | 8mg Mean Change DAS28-CRP From Baseline To Wks 76 and 128 |  |
|--------------------------------------|---|---|---|--|
| Subject group type                   | Subject analysis set                                      | Subject analysis set  | Subject analysis set                                      |  |
| Number of subjects analysed          | 107 <sup>[31]</sup>                                       | 61 <sup>[32]</sup>  | 31 <sup>[33]</sup>  |  |
| Units: units on a scale              |   |   |   |  |
| arithmetic mean (standard deviation) |   |   |   |  |
| Week 76 (n=107, 61, 31)              | -2.47 (± 1.23)  | -2.16 (± 1.28)  | -2.68 (± 1.12)  |  |
| Week 128 (n=79, 47, 18)              | -2.56 (± 1.16)  | -2.02 (± 1.23)  | -2.35 (± 1.4)   |  |

Notes:

[31] - Participants who received study drug in Parts C and D and had evaluable DAS28-CRP data.

[32] - Participants who received study drug in Parts C and D and had evaluable DAS28-CRP data.

[33] - Participants who received study drug in Parts C and D and had evaluable DAS28-CRP data.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Responders According to European League Against Rheumatism Responder Index Based on 28-Joint Count (EULAR28) Baseline through Weeks 12 and 24

|                 |   |
|-----------------|---|
| End point title | Percentage of Responders According to European League Against Rheumatism Responder Index Based on 28-Joint Count (EULAR28) Baseline through Weeks 12 and 24 |
|-----------------|---|

End point description:

EULAR28 categorizes clinical response based upon improvement since baseline in DAS modified to include the 28-joint count (DAS28) and post-baseline DAS28. DAS28 consists of a composite score of the following variables: TJC28, SJC28, CRP, and Patient's Global Assessment of their Disease Activity (patient's global VAS). DAS28 scores range from 1.0-9.4. EULAR28 categories include: No Response (improvement in DAS28 of  $\leq 0.6$  units or post-baseline DAS28 score  $> 5.1$  with improvement by  $\leq 1.2$  units), Moderate Response (post-baseline DAS28  $\leq 5.1$  with improvement by  $> 0.6$  units but  $\leq 1.2$  units or post-baseline DAS28 score  $> 3.2$  with improvement by  $> 1.2$  units), and Good Response (post-baseline DAS28 score  $\leq 3.2$  with improvement by  $> 1.2$  units).

Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated.  
9999=Data Not Available (N/A).

|                                  |           |
|----------------------------------|-----------|
| End point type                   | Secondary |
| End point timeframe:             |           |
| Baseline through Weeks 12 and 24 |           |

| End point values                  | 1 milligram (mg)<br>LY3009104 QD<br>- Part A | 2 mg<br>LY3009104 QD<br>- Parts A and B | 4 mg<br>LY3009104 QD<br>- Parts A and B | 8 mg<br>LY3009104 QD<br>- Parts A and B |
|-----------------------------------|--|---|---|---|
| Subject group type                | Reporting group                              | Reporting group                         | Reporting group                         | Reporting group                         |
| Number of subjects analysed       | 49 <sup>[34]</sup>                           | 52                                      | 52                                      | 50                                      |
| Units: percentage of participants |  |   |   |   |
| number (not applicable)           |  |   |   |   |
| Good Response - Week 12           | 22   | 17                                      | 46                                      | 40                                      |
| Moderate Response - Week 12       | 43   | 63                                      | 31                                      | 46                                      |
| No Response - Week 12             | 35   | 19                                      | 23                                      | 14                                      |
| Good Response - Week 24           | 9999   | 25                                      | 42                                      | 46                                      |
| Moderate Response - Week 24       | 9999   | 52                                      | 42                                      | 32                                      |
| No Response - Week 24             | 9999   | 23                                      | 15                                      | 22                                      |

Notes:

[34] - Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated.

| End point values                  | Placebo QD -<br>Part A |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 98 <sup>[35]</sup>     |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (not applicable)           |                        |  |  |  |
| Good Response - Week 12           | 16                     |  |  |  |
| Moderate Response - Week 12       | 35                     |  |  |  |
| No Response - Week 12             | 49                     |  |  |  |
| Good Response - Week 24           | 9999                   |  |  |  |
| Moderate Response - Week 24       | 9999                   |  |  |  |
| No Response - Week 24             | 9999                   |  |  |  |

Notes:

[35] - Participants were not dosed with placebo after Week 12; percentage was not calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Responders According to EULAR28 Baseline through Weeks 76 and 128

|                 |   |
|-----------------|---|
| End point title | Percentage of Responders According to EULAR28 Baseline through Weeks 76 and 128 |
|-----------------|---|

End point description:

EULAR28 categorizes clinical response based upon improvement since baseline in Disease Activity Score modified to include the 28-joint count (DAS28) and post-baseline DAS28. DAS28 consists of a composite score of the following variables: tender joint count (TJC28), swollen joint count (SJC28), CRP, and Patient's Global Assessment of their Disease Activity (patient's global VAS). DAS28 scores range from



1.0-9.4. EULAR28 categories include: No Response (improvement in DAS28 of  $\leq 0.6$  units or post-baseline DAS28 score  $> 5.1$  with improvement by  $\leq 1.2$  units), Moderate Response (post-baseline DAS28  $\leq 5.1$  with improvement by  $> 0.6$  units but  $\leq 1.2$  units or post-baseline DAS28 score  $> 3.2$  with improvement by  $> 1.2$  units), and Good Response (post-baseline DAS28 score  $\leq 3.2$  with improvement by  $> 1.2$  units).

All participants who received study drug in Parts C and D and had EULAR28 evaluated at analysis time points. LOCF was used to impute missing post-baseline values.

|                            |           |
|----------------------------|-----------|
| End point type             | Secondary |
| End point timeframe:       |           |
| Baseline, Weeks 76 and 128 |           |

| End point values                            | 4mg EULAR28 Response Wks 76 and 128 | 4-8mg EULAR28 Response Wks 76 and 128 | 8mg EULAR28 Response Wks 76 and 128 |  |
|---|-------------------------------------|---------------------------------------|-------------------------------------|--|
| Subject group type                          | Subject analysis set                | Subject analysis set                  | Subject analysis set                |  |
| Number of subjects analysed                 | 107                                 | 61                                    | 31                                  |  |
| Units: percentage of participants           |                                     |                                       |                                     |  |
| number (not applicable)                     |                                     |                                       |                                     |  |
| Good Response - Week 76 (n=107, 61, 31)     | 64                                  | 41                                    | 55                                  |  |
| Moderate Response - Week 76 (n=107, 61, 31) | 27                                  | 46                                    | 39                                  |  |
| No Response - Week 76 (n=107, 61, 31)       | 8                                   | 13                                    | 6                                   |  |
| Good Response - Week 128 (n=79, 47, 18)     | 65                                  | 40                                    | 56                                  |  |
| Moderate Response - Week 128 (n=79, 47, 18) | 30                                  | 40                                    | 28                                  |  |
| No Response - Week 128 (n=79, 47, 18)       | 5                                   | 19                                    | 17                                  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Meeting Low Disease Activity and Remission Based on the 28 Diarthrodial Joint Count (DAS28) Baseline through Weeks 12 and 24

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Meeting Low Disease Activity and Remission Based on the 28 Diarthrodial Joint Count (DAS28) Baseline through Weeks 12 and 24 |
|-----------------|---|

End point description:

Disease Activity Score (DAS) modified to include 28-joint count (DAS28) consisted of composite score of following variables: tender joint count (TJC28), swollen joint count (SJC28), CRP [milligrams per liter (mg/L)], and Patient's Global Assessment of Disease Activity using VAS (patient's global VAS). Scores ranged from 1.0-9.4, where lower scores indicated less disease activity. DAS28 scores  $\leq 3.2$  are considered as low disease activity, and scores  $< 2.6$  are considered as remission. Participants who discontinue before analysis time points are treated as non-responders.

Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated. 9999=Data Not Available (N/A).

|                                  |           |
|----------------------------------|-----------|
| End point type                   | Secondary |
| End point timeframe:             |           |
| Baseline through Weeks 12 and 24 |           |

| End point values                  | 1 milligram (mg)<br>LY3009104 QD<br>- Part A | 2 mg<br>LY3009104 QD<br>- Parts A and B | 4 mg<br>LY3009104 QD<br>- Parts A and B | 8 mg<br>LY3009104 QD<br>- Parts A and B |
|-----------------------------------|--|---|---|---|
| Subject group type                | Reporting group                              | Reporting group                         | Reporting group                         | Reporting group                         |
| Number of subjects analysed       | 49 <sup>[36]</sup>                           | 52                                      | 52                                      | 50                                      |
| Units: percentage of participants |  |   |   |   |
| number (not applicable)           |  |   |   |   |
| Low Disease Activity - Week 12    | 22   | 23                                      | 48                                      | 40                                      |
| Remission - Week 12               | 14   | 15                                      | 37                                      | 22                                      |
| Low Disease Activity - Week 24    | 9999   | 31                                      | 50                                      | 46                                      |
| Remission - Week 24               | 9999   | 15                                      | 33                                      | 36                                      |

Notes:

[36] - Participants were not dosed with 1 mg LY3009104 after Week 12; percentage was not calculated.

| End point values                  | Placebo QD -<br>Part A |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 98 <sup>[37]</sup>     |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (not applicable)           |                        |  |  |  |
| Low Disease Activity - Week 12    | 19                     |  |  |  |
| Remission - Week 12               | 4                      |  |  |  |
| Low Disease Activity - Week 24    | 9999                   |  |  |  |
| Remission - Week 24               | 9999                   |  |  |  |

Notes:

[37] - Participants were not dosed with placebo after Week 12; percentage was not calculated.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Meeting Low Disease Activity and Remission Based on the 28 Diarthrodial Joint Count (DAS28) Baseline through Weeks 76 and 128

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants Meeting Low Disease Activity and Remission Based on the 28 Diarthrodial Joint Count (DAS28) Baseline through Weeks 76 and 128 |
|-----------------|--|

End point description:

Disease Activity Score (DAS) modified to include 28 joint count (DAS28) consisted of composite score of following variables: tender joint count (TJC28), swollen joint count (SJC28), CRP (mg/L), and Patient's Global Assessment of Disease Activity using VAS (patient's global VAS). Scores ranged from 1.0-9.4, where lower scores indicated less disease activity. DAS28 scores  $\leq 3.2$  are considered as low disease activity, and scores  $< 2.6$  are considered as remission. Participants who discontinue before analysis time points are treated as non-responders.

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

End point timeframe:

Baseline through Weeks 76 and 128

| End point values                               | 4mg<br>Percentage<br>Participants<br>Meeting Low<br>DA Wks 76<br>and 128 | 4-8mg<br>Percentage<br>Participants<br>Meeting Low<br>DA Wks 76 and<br>128 | 8mg<br>Percentage<br>Participants<br>Meeting Low<br>DA Wks 76 and<br>128 |  |
|--|--|--|--|--|
| Subject group type                             | Subject analysis set   | Subject analysis set   | Subject analysis set   |  |
| Number of subjects analysed                    | 108  | 61   | 32   |  |
| Units: percentage of participants              |  |  |  |  |
| number (not applicable)                        |  |  |  |  |
| Low Disease activity - Week 76 (n=108, 61, 32) | 58   | 38   | 44   |  |
| Remission - Week 76 (n=108, 61, 32)            | 52   | 21   | 22   |  |
| Low Disease activity - Week 128 (n=79, 47, 18) | 59   | 36   | 56   |  |
| Remission - Week 128 (n=79, 47, 18)            | 47   | 26   | 39   |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change from Baseline through Week 12 in Duration (Minutes) of Morning Stiffness

|                 |  |
|-----------------|--|
| End point title | Mean Change from Baseline through Week 12 in Duration (Minutes) of Morning Stiffness |
|-----------------|--|

End point description:

The Investigator asked participants about the duration of their morning stiffness (in minutes) in and around the joints and recorded the duration. The Investigator asked the participants about duration of morning stiffness on the day prior to the study visit to capture actual symptoms. If morning stiffness duration was longer than 12 hours (720 minutes), it was truncated to 720 minutes for statistical presentations and analyses.

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

End point timeframe:

Baseline, Weeks 4, 8, 12

| End point values                     | 1 milligram<br>(mg)<br>LY3009104 QD<br>- Part A | 2 mg<br>LY3009104 QD<br>- Parts A and B | 4 mg<br>LY3009104 QD<br>- Parts A and B | 8 mg<br>LY3009104 QD<br>- Parts A and B |
|--------------------------------------|---|---|---|---|
| Subject group type                   | Reporting group                                 | Reporting group                         | Reporting group                         | Reporting group                         |
| Number of subjects analysed          | 48 <sup>[38]</sup>                              | 51 <sup>[39]</sup>                      | 50 <sup>[40]</sup>                      | 50                                      |
| Units: minutes                       |   |   |   |   |
| arithmetic mean (standard deviation) |   |   |   |   |
| Week 4 (n=47, 50, 50, 50, 94)        | -34.1 (± 70.49)                                 | -27 (± 46.49)                           | -57.4 (± 149)                           | -25.5 (± 126.13)                        |

|                                |                 |                 |                  |                  |
|--------------------------------|-----------------|-----------------|------------------|------------------|
| Week 8 (n=46, 50, 50, 50, 86)  | -41.2 (± 85.45) | -31.1 (± 45.8)  | -67.8 (± 138.02) | -53.8 (± 101.76) |
| Week 12 (n=48, 51, 50, 50, 97) | -49.5 (± 72.8)  | -30.7 (± 47.41) | -75 (± 142.04)   | -62.7 (± 88.27)  |

Notes:

[38] - Participants who received study drug in Part A and had evaluable morning stiffness data.

[39] - Participants who received study drug in Part A and had evaluable morning stiffness data.

[40] - Participants who received study drug in Part A and had evaluable morning stiffness data.

| End point values                     | Placebo QD - Part A |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 97 <sup>[41]</sup>  |  |  |  |
| Units: minutes                       |                     |  |  |  |
| arithmetic mean (standard deviation) |                     |  |  |  |
| Week 4 (n=47, 50, 50, 50, 94)        | -22.5 (± 63.61)     |  |  |  |
| Week 8 (n=46, 50, 50, 50, 86)        | -25.5 (± 67.39)     |  |  |  |
| Week 12 (n=48, 51, 50, 50, 97)       | -33.9 (± 97.79)     |  |  |  |

Notes:

[41] - Participants who received study drug in Part A and had evaluable morning stiffness data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline to Week 12 in Medical Outcomes Study 36-Item Short Form (SF-36) Health Survey Physical Component Summary (PCS) and Mental Component Summary (MCS) Scores

|                 |  |
|-----------------|--|
| End point title | Mean Change from Baseline to Week 12 in Medical Outcomes Study 36-Item Short Form (SF-36) Health Survey Physical Component Summary (PCS) and Mental Component Summary (MCS) Scores |
|-----------------|--|

End point description:

The SF-36 is a health-related survey that assesses participant's quality of life and consists of 36 questions covering 8 health domains (physical functioning, bodily pain, role limitations due to physical problems and also emotional problems, general health, mental health, social functioning and vitality) and 2 component scores (PCS and MCS). The PCS score consisted of physical functioning, bodily pain, role-physical, and general health scales. The MCS score consisted of social functioning, vitality, mental health, and role-emotional scales. Both PCS and MCS range from 0-100 with higher scores indicating better health or functioning.

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

End point timeframe:

Baseline, Week 12

| End point values            | 1 milligram (mg) LY3009104 QD - Part A | 2 mg LY3009104 QD - Parts A and B | 4 mg LY3009104 QD - Parts A and B | 8 mg LY3009104 QD - Parts A and B |
|-----------------------------|--|-----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type          | Reporting group                        | Reporting group                   | Reporting group                   | Reporting group                   |
| Number of subjects analysed | 48 <sup>[42]</sup>                     | 51 <sup>[43]</sup>                | 51 <sup>[44]</sup>                | 50                                |
| Units: units on a scale     |  |                                   |                                   |                                   |

|                                      |                 |                |                |                 |
|--------------------------------------|-----------------|----------------|----------------|-----------------|
| arithmetic mean (standard deviation) |                 |                |                |                 |
| PCS                                  | 6.66 (± 8.074)  | 4.15 (± 7.68)  | 7.07 (± 7.378) | 7 (± 9.054)     |
| MCS                                  | 2.54 (± 11.983) | 1.89 (± 6.869) | 2.39 (± 7.898) | 3.03 (± 10.675) |

Notes:

[42] - Participants who received study drug in Part A and had evaluable SF-36 data.

[43] - Participants who received study drug in Part A and had evaluable SF-36 data.

[44] - Participants who received study drug in Part A and had evaluable SF-36 data.

|                                      |                     |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| <b>End point values</b>              | Placebo QD - Part A |  |  |  |
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 97 <sup>[45]</sup>  |  |  |  |
| Units: units on a scale              |                     |  |  |  |
| arithmetic mean (standard deviation) |                     |  |  |  |
| PCS                                  | 3.22 (± 6.733)      |  |  |  |
| MCS                                  | 0.88 (± 10.437)     |  |  |  |

Notes:

[45] - Participants who received study drug in Part A and had evaluable SF-36 data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline to Week 12 in Brief Pain Inventory Modified Short Form (BPI-SF Modified) Worst-Pain-in-the-Past-24-hours Item Score

|                 |   |
|-----------------|---|
| End point title | Mean Change from Baseline to Week 12 in Brief Pain Inventory Modified Short Form (BPI-SF Modified) Worst-Pain-in-the-Past-24-hours Item Score |
|-----------------|---|

End point description:

The BPI-sf modified is a self-administered questionnaire developed for the rapid assessment of pain. The BPI-sf modified provides information on the intensity of pain (the sensory dimension) as well as the degree to which pain interferes with function (the reactive dimension). The questionnaire asks questions about pain relief, pain quality, and the participant's perception of the cause of pain. The BPI-sf modified uses a numeric rating scale from 0 ("No pain") to 10 ("Pain as bad as you can imagine"). Since pain can be quite variable over a day, the BPI-sf modified asked participants to rate their pain at the time of responding to the questionnaire (right now), and also at its worst, least and average over the last 24 hours.

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

End point timeframe:

Baseline, Week 12

|                                      |   |                                      |                                      |                                      |
|--------------------------------------|---|--------------------------------------|--------------------------------------|--------------------------------------|
| <b>End point values</b>              | 1 milligram (mg)<br>LY3009104 QD - Part A | 2 mg<br>LY3009104 QD - Parts A and B | 4 mg<br>LY3009104 QD - Parts A and B | 8 mg<br>LY3009104 QD - Parts A and B |
| Subject group type                   | Reporting group                           | Reporting group                      | Reporting group                      | Reporting group                      |
| Number of subjects analysed          | 48 <sup>[46]</sup>                        | 51 <sup>[47]</sup>                   | 51 <sup>[48]</sup>                   | 50                                   |
| Units: units on a scale              |   |                                      |                                      |                                      |
| arithmetic mean (standard deviation) | -1.35 (± 2.547)                           | -0.67 (± 2.132)                      | -1.41 (± 1.813)                      | -1.54 (± 2.131)                      |

Notes:

[46] - Participants who received study drug and had evaluable BPI-sf worst-pain-in-the past-24-hours data.

[47] - Participants who received study drug and had evaluable BPI-sf worst-pain-in-the past-24-hours data.

[48] - Participants who received study drug and had evaluable BPI-sf worst-pain-in-the past-24-hours data.

|                                      |                     |  |  |  |
|--------------------------------------|---------------------|--|--|--|
| <b>End point values</b>              | Placebo QD - Part A |  |  |  |
| Subject group type                   | Reporting group     |  |  |  |
| Number of subjects analysed          | 97 <sup>[49]</sup>  |  |  |  |
| Units: units on a scale              |                     |  |  |  |
| arithmetic mean (standard deviation) | -0.35 (± 2.136)     |  |  |  |

Notes:

[49] - Participants who received study drug and had evaluable BPI-sf worst-pain-in-the past-24-hours data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline to Week 12 in Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F) Score

|                 |  |
|-----------------|--|
| End point title | Mean Change from Baseline to Week 12 in Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F) Score |
|-----------------|--|

End point description:

The FACIT-F Scale is a brief 13-item, symptom-specific questionnaire that specifically assesses the participant self-reported severity of fatigue and its impact upon daily activities and functioning. The FACIT-F uses a numeric rating scale of 0 ("Not at all") to 4 ("Very much") for each item to assess fatigue and its impact in the past 7 days. Total scores range from 0 to 52, with higher scores indicating less fatigue.

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

End point timeframe:

Baseline, Week 12

|                                      |  |                                   |                                   |                                   |
|--------------------------------------|--|-----------------------------------|-----------------------------------|-----------------------------------|
| <b>End point values</b>              | 1 milligram (mg) LY3009104 QD - Part A | 2 mg LY3009104 QD - Parts A and B | 4 mg LY3009104 QD - Parts A and B | 8 mg LY3009104 QD - Parts A and B |
| Subject group type                   | Reporting group                        | Reporting group                   | Reporting group                   | Reporting group                   |
| Number of subjects analysed          | 48 <sup>[50]</sup>                     | 51 <sup>[51]</sup>                | 51 <sup>[52]</sup>                | 50                                |
| Units: units on a scale              |  |                                   |                                   |                                   |
| arithmetic mean (standard deviation) | 4.48 (± 10.492)                        | 3.8 (± 9.152)                     | 4.41 (± 8.631)                    | 4.11 (± 9.971)                    |

Notes:

[50] - Participants who received study drug in Part A and had evaluable FACIT-F at Week 12 data.

[51] - Participants who received study drug in Part A and had evaluable FACIT-F at Week 12 data.

[52] - Participants who received study drug in Part A and had evaluable FACIT-F at Week 12 data.

|                         |                     |  |  |  |
|-------------------------|---------------------|--|--|--|
| <b>End point values</b> | Placebo QD - Part A |  |  |  |
|-------------------------|---------------------|--|--|--|

|                                      |                    |  |  |  |
|--------------------------------------|--------------------|--|--|--|
| Subject group type                   | Reporting group    |  |  |  |
| Number of subjects analysed          | 97 <sup>[53]</sup> |  |  |  |
| Units: units on a scale              |                    |  |  |  |
| arithmetic mean (standard deviation) | 2.02 (± 8.941)     |  |  |  |

Notes:

[53] - Participants who received study drug in Part A and had evaluable FACIT-F at Week 12 data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Population Pharmacokinetics (PK): Maximum Concentration at Steady State of Dosing (C<sub>max,ss</sub>) of LY3009104

|                 |   |
|-----------------|---|
| End point title | Population Pharmacokinetics (PK): Maximum Concentration at Steady State of Dosing (C <sub>max,ss</sub> ) of LY3009104 <sup>[54]</sup> |
|-----------------|---|

End point description:

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

End point timeframe:

Baseline through 24 weeks

Notes:

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All randomized participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data. Participants receiving placebo will not have PK data.

| End point values                                    | 1 milligram (mg)<br>LY3009104 QD<br>- Part A | 2mg<br>LY3009104 PK<br>Assessment for<br>C <sub>max</sub> Part A | 4mg<br>LY3009104 PK<br>Assessment for<br>C <sub>max</sub> Part A | 8mg<br>LY3009104 PK<br>Assessment for<br>C <sub>max</sub> Part A |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                              | Subject analysis set   | Subject analysis set   | Subject analysis set   |
| Number of subjects analysed                         | 47 <sup>[55]</sup>                           | 91 <sup>[56]</sup>   | 91 <sup>[57]</sup>   | 50   |
| Units: nanomoles/Liter (nmol/L)                     |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 36.5 (± 36.1)                                | 59.1 (± 21.3)  | 119 (± 20.5)   | 241 (± 22.9)   |

Notes:

[55] - Participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

[56] - Participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

[57] - Participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Population PK: Area Under the Concentration Curve Versus Time at a Dosing Interval at Steady State (AUC<sub>tau,ss</sub>) of LY3009104

|                 |  |
|-----------------|--|
| End point title | Population PK: Area Under the Concentration Curve Versus Time at a Dosing Interval at Steady State (AUC <sub>tau,ss</sub> ) of LY3009104 <sup>[58]</sup> |
|-----------------|--|

End point description:

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

End point timeframe:

Baseline through 24 weeks

Notes:

[58] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: All randomized participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data. Participants receiving placebo will not have PK data.

| End point values                                    | 1 milligram (mg) LY3009104 QD - Part A | 2mg LY3009104 PK Assessment for AUC Part A | 4mg LY3009104 PK Assessment for AUC Part A | 8mg LY3009104 PK Assessment for AUC Part A |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                        | Subject analysis set                       | Subject analysis set                       | Subject analysis set                       |
| Number of subjects analysed                         | 47 <sup>[59]</sup>                     | 91 <sup>[60]</sup>                         | 91 <sup>[61]</sup>                         | 50   |
| Units: nanomoles*hour/Liter (nmol*h/L)              |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 333 (± 61.7)                           | 541 (± 38)                                 | 1060 (± 37)                                | 2190 (± 45.6)                              |

Notes:

[59] - Participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

[60] - Participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

[61] - Participants who received at least 1 dose of LY3009104 with evaluable LY3009104 PK data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline through Week 12 in the Ensemble Minimum Data Set 1.0

|                 |  |
|-----------------|--|
| End point title | Mean Change from Baseline through Week 12 in the Ensemble Minimum Data Set 1.0 |
|-----------------|--|

End point description:

Zero participants were analyzed. Assessment of Ensemble Minimum Data Set 1.0 was not collected at Week 12 and therefore results are not reported for outcome measure.

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

End point timeframe:

Baseline, 12 weeks

| End point values            | 1 milligram (mg) LY3009104 QD - Part A | 2 mg LY3009104 QD - Parts A and B | 4 mg LY3009104 QD - Parts A and B | 8 mg LY3009104 QD - Parts A and B |
|-----------------------------|--|-----------------------------------|-----------------------------------|-----------------------------------|
| Subject group type          | Reporting group                        | Reporting group                   | Reporting group                   | Reporting group                   |
| Number of subjects analysed | 0 <sup>[62]</sup>                      | 0 <sup>[63]</sup>                 | 0 <sup>[64]</sup>                 | 0 <sup>[65]</sup>                 |
| Units: number               |  |                                   |                                   |                                   |
| number (not applicable)     |  |                                   |                                   |                                   |

Notes:

[62] - Zero participants were analyzed. Assessment of Ensemble Minimum Data Set 1.0 was not collected.

[63] - Zero participants were analyzed. Assessment of Ensemble Minimum Data Set 1.0 was not collected.

[64] - Zero participants were analyzed. Assessment of Ensemble Minimum Data Set 1.0 was not collected.

[65] - Zero participants were analyzed. Assessment of Ensemble Minimum Data Set 1.0 was not collected.

|                  |              |  |  |  |
|------------------|--------------|--|--|--|
| End point values | Placebo QD - |  |  |  |
|------------------|--------------|--|--|--|



|                             |                   |  |  |  |
|-----------------------------|-------------------|--|--|--|
|                             | Part A            |  |  |  |
| Subject group type          | Reporting group   |  |  |  |
| Number of subjects analysed | 0 <sup>[66]</sup> |  |  |  |
| Units: number               |                   |  |  |  |
| number (not applicable)     |                   |  |  |  |

Notes:

[66] - Zero participants were analyzed. Assessment of Ensemble Minimum Data Set 1.0 was not collected.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

I4V-MC-JADA

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

### Reporting groups

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | 1 mg LY3009104 once daily Weeks 0-12 |
|-----------------------|--------------------------------------|

Reporting group description: -

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | 2 mg LY3009104 once daily Weeks 0-12 |
|-----------------------|--------------------------------------|

Reporting group description: -

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | 4 mg LY3009104 once daily Weeks 0-12 |
|-----------------------|--------------------------------------|

Reporting group description: -

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | 8 mg LY3009104 once daily Weeks 0-12 |
|-----------------------|--------------------------------------|

Reporting group description: -

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Placebo once daily Weeks 0-12 |
|-----------------------|-------------------------------|

Reporting group description: -

|                       |  |
|-----------------------|--|
| Reporting group title | 2 mg LY3009104 twice daily crossover Weeks 12-24 |
|-----------------------|--|

Reporting group description: -

|                       |   |
|-----------------------|---|
| Reporting group title | 4 mg LY3009104 once daily crossover Weeks 12-24 |
|-----------------------|---|

Reporting group description: -

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | 2 mg LY3009104 once daily Weeks 12-24 |
|-----------------------|---------------------------------------|

Reporting group description: -

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | 4 mg LY3009104 once daily Weeks 12-24 |
|-----------------------|---------------------------------------|

Reporting group description: -

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | 8 mg LY3009104 once daily Weeks 12-24 |
|-----------------------|---------------------------------------|

Reporting group description: -

|                       |   |
|-----------------------|---|
| Reporting group title | 4/4 mg LY3009104 once daily Weeks 24-76 |
|-----------------------|---|

Reporting group description: -

|                       |  |
|-----------------------|--|
| Reporting group title | 4:8/4 mg LY3009104 once daily pre-rescue Weeks 24-76 |
|-----------------------|--|

Reporting group description: -

|                       |   |
|-----------------------|---|
| Reporting group title | 4:8/4 mg LY3009104 once daily post-rescue Weeks 24-76 |
|-----------------------|---|

Reporting group description: -

|                       |   |
|-----------------------|---|
| Reporting group title | 8/4 mg LY3009104 once daily Weeks 24-76 |
|-----------------------|---|

Reporting group description: -

|                       |  |
|-----------------------|--|
| Reporting group title | 4/4 mg LY3009104 once daily Weeks 76-128 |
|-----------------------|--|

Reporting group description: -

|                       |  |
|-----------------------|--|
| Reporting group title | 4:8/4 mg LY3009104 once daily Weeks 76-128 |
|-----------------------|--|

Reporting group description: -

|                       |  |
|-----------------------|--|
| Reporting group title | 8/4 mg LY3009104 once daily Weeks 76-128 |
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Reporting group description: -

|                       |           |
|-----------------------|-----------|
| Reporting group title | Follow-up |
|-----------------------|-----------|

Reporting group description: -

| <b>Serious adverse events</b>                                       | 1 mg LY3009104<br>once daily Weeks 0-12 | 2 mg LY3009104<br>once daily Weeks 0-12 | 4 mg LY3009104<br>once daily Weeks 0-12 |
|---|---|---|---|
| Total subjects affected by serious adverse events                   |   |   |   |
| subjects affected / exposed   | 0 / 49 (0.00%)                          | 3 / 52 (5.77%)                          | 2 / 52 (3.85%)                          |
| number of deaths (all causes)                                       | 0                                       | 0                                       | 0                                       |
| number of deaths resulting from adverse events                      | 0                                       | 0                                       | 0                                       |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |   |   |
| basal cell carcinoma  |   |   |   |
| alternative dictionary used: MedDRA 16.1                            |   |   |   |
| subjects affected / exposed   | 0 / 49 (0.00%)                          | 0 / 52 (0.00%)                          | 0 / 52 (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                                   |
| Pregnancy, puerperium and perinatal conditions                      |   |   |   |
| abortion spontaneous  |   |   |   |
| alternative dictionary used: MedDRA 16.1                            |   |   |   |
| subjects affected / exposed <sup>[1]</sup>                          | 0 / 42 (0.00%)                          | 0 / 44 (0.00%)                          | 0 / 37 (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                                   |
| pregnancy   |   |   |   |
| alternative dictionary used: MedDRA 16.1                            |   |   |   |
| subjects affected / exposed <sup>[2]</sup>                          | 0 / 42 (0.00%)                          | 0 / 44 (0.00%)                          | 0 / 37 (0.00%)                          |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                   | 0 / 0                                   |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                   | 0 / 0                                   |
| General disorders and administration site conditions                |   |   |   |
| non-cardiac chest pain  |   |   |   |
| alternative dictionary used: MedDRA 16.1                            |   |   |   |
| subjects affected / exposed   | 0 / 49 (0.00%)                          | 0 / 52 (0.00%)                          | 0 / 52 (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                                   |
| pyrexia   |   |   |   |
| alternative dictionary used: MedDRA 16.1                            |   |   |   |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| asthma  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (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          |
| pneumothorax                                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |                |                |                |
| major depression                                |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| alanine aminotransferase increased              |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| aspartate aminotransferase increased            |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| blood creatine phosphokinase increased          |                |                |                |
| alternative dictionary used:                    |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| MedDRA 16.1                                     |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| glomerular filtration rate decreased            |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| hepatic enzyme increased                        |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| transaminases increased                         |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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 dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| head injury                                     |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| jaw fracture                                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (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          |
| rib fracture                                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| road traffic accident                           |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| scar  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| myocardial infarction                           |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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                        |                |                |                |
| carotid artery stenosis                         |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| presyncope                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| syncope   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| anaemia   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| microcytic anaemia                              |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| normochromic normocytic anaemia                 |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| pancytopenia                                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| cataract  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| ulcerative keratitis                            |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| coeliac disease                                 |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| colitis   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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 dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| large intestinal obstruction                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| large intestinal stenosis                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| cholecystitis                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| cholelithiasis                                  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |                |                |                |
| angioedema                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| haematuria                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| renal failure                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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 |                |                |                |
| arthritis                                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| diastasis recti abdominis<br>alternative dictionary used:<br>MedDRA 16.1      |                |                |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all                               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                    | 0 / 0          | 0 / 0          | 0 / 0          |
| intervertebral disc protrusion<br>alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| neck pain<br>alternative dictionary used:<br>MedDRA 16.1                      |                |                |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| osteoarthritis<br>alternative dictionary used:<br>MedDRA 16.1                 |                |                |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all                               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations   |                |                |                |
| acute hepatitis b<br>alternative dictionary used:<br>MedDRA 16.1              |                |                |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| bronchitis<br>alternative dictionary used:<br>MedDRA 16.1                     |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| gastroenteritis                                 |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| gastroenteritis viral                           |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (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          |
| helicobacter gastritis                          |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| herpes simplex                                  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| herpes zoster                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pneumonia                                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 52 (1.92%) | 0 / 52 (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 bacterial<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed                               | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders<br>dehydration<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| hyperglycaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed                                    | 0 / 49 (0.00%) | 0 / 52 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>  | 8 mg LY3009104<br>once daily Weeks 0-12 | Placebo once daily<br>Weeks 0-12 | 2 mg LY3009104<br>twice daily crossover<br>Weeks 12-24 |
|--|---|----------------------------------|--|
| Total subjects affected by serious<br>adverse events   |   |                                  |  |
| subjects affected / exposed  | 1 / 50 (2.00%)                          | 3 / 98 (3.06%)                   | 2 / 63 (3.17%)   |
| number of deaths (all causes)  | 0                                       | 0                                | 0  |
| number of deaths resulting from<br>adverse events  | 0                                       | 0                                | 0  |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps)<br>basal cell carcinoma<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed | 0 / 50 (0.00%)                          | 0 / 98 (0.00%)                   | 0 / 63 (0.00%)   |
| occurrences causally related to<br>treatment / all   | 0 / 0                                   | 0 / 0                            | 0 / 0  |
| deaths causally related to<br>treatment / all  | 0 / 0                                   | 0 / 0                            | 0 / 0  |
| Pregnancy, puerperium and perinatal<br>conditions<br>abortion spontaneous<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed <sup>[1]</sup>       | 0 / 41 (0.00%)                          | 0 / 85 (0.00%)                   | 0 / 56 (0.00%)   |
| occurrences causally related to<br>treatment / all   | 0 / 0                                   | 0 / 0                            | 0 / 0  |
| deaths causally related to<br>treatment / all  | 0 / 0                                   | 0 / 0                            | 0 / 0  |

|  |                                  |                                  |                                  |
|--|----------------------------------|----------------------------------|----------------------------------|
| pregnancy<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed <sup>[2]</sup><br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 41 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 85 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 56 (0.00%)<br>0 / 0<br>0 / 0 |
| General disorders and administration<br>site conditions<br>non-cardiac chest pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all | 0 / 50 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 98 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 63 (0.00%)<br>0 / 0<br>0 / 0 |
| pyrexia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 50 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 98 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 63 (1.59%)<br>0 / 1<br>0 / 0 |
| Respiratory, thoracic and mediastinal<br>disorders<br>asthma<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all                      | 0 / 50 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 98 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 63 (0.00%)<br>0 / 0<br>0 / 0 |
| pneumothorax<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all  | 0 / 50 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 98 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 63 (0.00%)<br>0 / 0<br>0 / 0 |
| Psychiatric disorders<br>major depression<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences causally related to<br>treatment / all<br>deaths causally related to<br>treatment / all   | 0 / 50 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 98 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 63 (0.00%)<br>0 / 0<br>0 / 0 |

|  |                |                |                |
|--|----------------|----------------|----------------|
| Investigations                                     |                |                |                |
| alanine aminotransferase increased                 |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| aspartate aminotransferase<br>increased            |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| blood creatine phosphokinase<br>increased          |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| glomerular filtration rate decreased               |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| hepatic enzyme increased                           |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| transaminases increased                            |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural<br>complications  |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| fall   |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| head injury  |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| jaw fracture                                       |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| rib fracture                                       |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| road traffic accident                              |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| scar   |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                                  |                |                |                |
| myocardial infarction                              |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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                        |                |                |                |
| carotid artery stenosis                         |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| presyncope                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| syncope   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| anaemia   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| microcytic anaemia                              |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 98 (1.02%) | 0 / 63 (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          |
| normochromic normocytic anaemia                 |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| pancytopenia                                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 1 / 50 (2.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| Eye disorders                                   |                |                |                |
| cataract  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| ulcerative keratitis                            |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| coeliac disease                                 |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 98 (1.02%) | 0 / 63 (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          |
| colitis   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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 dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed   | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| large intestinal obstruction<br>alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed   | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| large intestinal stenosis<br>alternative dictionary used:<br>MedDRA 16.1    |                |                |                |
| subjects affected / exposed   | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                  | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders   |                |                |                |
| cholecystitis<br>alternative dictionary used:<br>MedDRA 16.1                |                |                |                |
| subjects affected / exposed   | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all                             | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                                  | 0 / 0          | 0 / 0          | 0 / 0          |
| cholelithiasis<br>alternative dictionary used:<br>MedDRA 16.1               |                |                |                |
| subjects affected / exposed   | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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                                      |                |                |                |
| angioedema<br>alternative dictionary used:<br>MedDRA 16.1                   |                |                |                |
| subjects affected / exposed   | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                  | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders   |                |                |                |
| haematuria<br>alternative dictionary used:<br>MedDRA 16.1                   |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 98 (1.02%) | 0 / 63 (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                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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 |                |                |                |
| arthritis                                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| diastasis recti abdominis                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| intervertebral disc protrusion                  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| neck pain                                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| osteoarthritis                                  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| acute hepatitis b                               |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| bronchitis                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| gastroenteritis                                 |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| gastroenteritis viral                           |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| helicobacter gastritis                          |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| herpes simplex                                  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| herpes zoster                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pneumonia                                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pneumonia bacterial                             |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| Metabolism and nutrition disorders              |                |                |                |
| dehydration                                     |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (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          |
| hyperglycaemia                                  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 50 (0.00%) | 1 / 98 (1.02%) | 0 / 63 (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          |

|   |   |   |   |
|---|---|---|---|
| <b>Serious adverse events</b>                     | 4 mg LY3009104<br>once daily crossover<br>Weeks 12-24 | 2 mg LY3009104<br>once daily Weeks<br>12-24 | 4 mg LY3009104<br>once daily Weeks<br>12-24 |
| Total subjects affected by serious adverse events |   |   |   |
| subjects affected / exposed                       | 1 / 63 (1.59%)  | 0 / 51 (0.00%)                              | 0 / 50 (0.00%)                              |

|   |                |                |                |
|---|----------------|----------------|----------------|
| number of deaths (all causes)                                       | 0              | 0              | 0              |
| number of deaths resulting from adverse events                      | 0              | 0              | 0              |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                |
| basal cell carcinoma  |                |                |                |
| alternative dictionary used: MedDRA 16.1                            |                |                |                |
| subjects affected / exposed   | 1 / 63 (1.59%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| Pregnancy, puerperium and perinatal conditions                      |                |                |                |
| abortion spontaneous  |                |                |                |
| alternative dictionary used: MedDRA 16.1                            |                |                |                |
| subjects affected / exposed <sup>[1]</sup>                          | 0 / 54 (0.00%) | 0 / 43 (0.00%) | 0 / 35 (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          |
| pregnancy   |                |                |                |
| alternative dictionary used: MedDRA 16.1                            |                |                |                |
| subjects affected / exposed <sup>[2]</sup>                          | 0 / 54 (0.00%) | 0 / 43 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions                |                |                |                |
| non-cardiac chest pain  |                |                |                |
| alternative dictionary used: MedDRA 16.1                            |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| pyrexia   |                |                |                |
| alternative dictionary used: MedDRA 16.1                            |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders                     |                |                |                |
| asthma  |                |                |                |
| alternative dictionary used: MedDRA 16.1                            |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| pneumothorax                                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |                |                |                |
| major depression                                |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| alanine aminotransferase increased              |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| aspartate aminotransferase increased            |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| blood creatine phosphokinase increased          |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| glomerular filtration rate decreased            |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| hepatic enzyme increased<br>alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| transaminases increased<br>alternative dictionary used:<br>MedDRA 16.1  |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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<br>alternative dictionary used:<br>MedDRA 16.1                     |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| head injury<br>alternative dictionary used:<br>MedDRA 16.1              |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| jaw fracture<br>alternative dictionary used:<br>MedDRA 16.1             |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| rib fracture<br>alternative dictionary used:<br>MedDRA 16.1             |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| road traffic accident                           |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| scar  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| myocardial infarction                           |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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                        |                |                |                |
| carotid artery stenosis                         |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| presyncope                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| syncope   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| anaemia   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| microcytic anaemia                              |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| normochromic normocytic anaemia                 |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| pancytopenia                                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| cataract  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| ulcerative keratitis                            |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| coeliac disease                                 |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| colitis   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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 dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| large intestinal obstruction                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| large intestinal stenosis                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| cholecystitis                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| cholelithiasis                                  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |                |                |                |
| angioedema                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| haematuria                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| renal failure                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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 |                |                |                |
| arthritis                                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| diastasis recti abdominis                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all                               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                    | 0 / 0          | 0 / 0          | 0 / 0          |
| intervertebral disc protrusion<br>alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| neck pain<br>alternative dictionary used:<br>MedDRA 16.1                      |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| osteoarthritis<br>alternative dictionary used:<br>MedDRA 16.1                 |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all                               | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations   |                |                |                |
| acute hepatitis b<br>alternative dictionary used:<br>MedDRA 16.1              |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| bronchitis<br>alternative dictionary used:<br>MedDRA 16.1                     |                |                |                |
| subjects affected / exposed   | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| gastroenteritis<br>alternative dictionary used:<br>MedDRA 16.1                |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| gastroenteritis viral                           |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |
| helicobacter gastritis                          |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| herpes simplex                                  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| herpes zoster                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pneumonia                                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pneumonia bacterial                             |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (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          |

|  |                |                |                |
|--|----------------|----------------|----------------|
| Metabolism and nutrition disorders                 |                |                |                |
| dehydration  |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| hyperglycaemia                                     |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                |                |
| subjects affected / exposed                        | 0 / 63 (0.00%) | 0 / 51 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|  |   |   |   |
|--|---|---|---|
| <b>Serious adverse events</b>  | 8 mg LY3009104<br>once daily Weeks<br>12-24 | 4/4 mg LY3009104<br>once daily Weeks<br>24-76 | 4:8/4 mg<br>LY3009104 once<br>daily pre-rescue<br>Weeks 24-76 |
| Total subjects affected by serious<br>adverse events                   |   |   |   |
| subjects affected / exposed  | 3 / 49 (6.12%)                              | 16 / 108 (14.81%)                             | 1 / 61 (1.64%)  |
| number of deaths (all causes)  | 0   | 0   | 0   |
| number of deaths resulting from<br>adverse events                      | 0   | 0   | 0   |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |   |   |   |
| basal cell carcinoma   |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1                            |   |   |   |
| subjects affected / exposed  | 0 / 49 (0.00%)                              | 0 / 108 (0.00%)                               | 0 / 61 (0.00%)  |
| occurrences causally related to<br>treatment / all                     | 0 / 0                                       | 0 / 0   | 0 / 0   |
| deaths causally related to<br>treatment / all                          | 0 / 0                                       | 0 / 0   | 0 / 0   |
| Pregnancy, puerperium and perinatal<br>conditions                      |   |   |   |
| abortion spontaneous   |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1                            |   |   |   |
| subjects affected / exposed <sup>[1]</sup>                             | 0 / 40 (0.00%)                              | 0 / 87 (0.00%)                                | 0 / 52 (0.00%)  |
| occurrences causally related to<br>treatment / all                     | 0 / 0                                       | 0 / 0   | 0 / 0   |
| deaths causally related to<br>treatment / all                          | 0 / 0                                       | 0 / 0   | 0 / 0   |
| pregnancy  |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1                            |   |   |   |

|  |                |                 |                |
|--|----------------|-----------------|----------------|
| subjects affected / exposed <sup>[2]</sup>           | 0 / 40 (0.00%) | 0 / 87 (0.00%)  | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0          |
| General disorders and administration site conditions |                |                 |                |
| non-cardiac chest pain                               |                |                 |                |
| alternative dictionary used: MedDRA 16.1             |                |                 |                |
| subjects affected / exposed                          | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| pyrexia  |                |                 |                |
| alternative dictionary used: MedDRA 16.1             |                |                 |                |
| subjects affected / exposed                          | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders      |                |                 |                |
| asthma   |                |                 |                |
| alternative dictionary used: MedDRA 16.1             |                |                 |                |
| subjects affected / exposed                          | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| pneumothorax   |                |                 |                |
| alternative dictionary used: MedDRA 16.1             |                |                 |                |
| subjects affected / exposed                          | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0          |
| Psychiatric disorders                                |                |                 |                |
| major depression                                     |                |                 |                |
| alternative dictionary used: MedDRA 16.1             |                |                 |                |
| subjects affected / exposed                          | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0           | 0 / 0          |
| Investigations                                       |                |                 |                |
| alanine aminotransferase increased                   |                |                 |                |



|  |                |                 |                |
|--|----------------|-----------------|----------------|
| alternative dictionary used:<br>MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                        | 0 / 49 (0.00%) | 2 / 108 (1.85%) | 0 / 61 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 1 / 2           | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| aspartate aminotransferase<br>increased            |                |                 |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                        | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| blood creatine phosphokinase<br>increased          |                |                 |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                        | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| glomerular filtration rate decreased               |                |                 |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                        | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| hepatic enzyme increased                           |                |                 |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                        | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| transaminases increased                            |                |                 |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                        | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 1 / 1           | 0 / 0          |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Injury, poisoning and procedural<br>complications  |                |                 |                |
| fall   |                |                 |                |
| alternative dictionary used:<br>MedDRA 16.1        |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| head injury                                     |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (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          |
| jaw fracture                                    |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| rib fracture                                    |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| road traffic accident                           |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (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          |
| scar  |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Cardiac disorders                               |                |                 |                |
| myocardial infarction                           |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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                        |                |                 |                |
| carotid artery stenosis                         |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (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          |
| presyncope                                      |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| syncope   |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Blood and lymphatic system disorders            |                |                 |                |
| anaemia   |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (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          |
| microcytic anaemia                              |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| normochromic normocytic anaemia                 |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| pancytopenia                                    |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Eye disorders                                   |                |                 |                |
| cataract  |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (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          |
| ulcerative keratitis                            |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Gastrointestinal disorders                      |                |                 |                |
| coeliac disease                                 |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| colitis   |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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 dictionary used: MedDRA 16.1        |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| large intestinal obstruction<br>alternative dictionary used:<br>MedDRA 16.1 |                |                 |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| large intestinal stenosis<br>alternative dictionary used:<br>MedDRA 16.1    |                |                 |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all                                  | 0 / 0          | 0 / 0           | 0 / 0          |
| Hepatobiliary disorders   |                |                 |                |
| cholecystitis<br>alternative dictionary used:<br>MedDRA 16.1                |                |                 |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| cholelithiasis<br>alternative dictionary used:<br>MedDRA 16.1               |                |                 |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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                                      |                |                 |                |
| angioedema<br>alternative dictionary used:<br>MedDRA 16.1                   |                |                 |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (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   |                |                 |                |
| haematuria<br>alternative dictionary used:<br>MedDRA 16.1                   |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| renal failure                                   |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| Musculoskeletal and connective tissue disorders |                |                 |                |
| arthritis                                       |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (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          |
| diastasis recti abdominis                       |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| intervertebral disc protrusion                  |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| neck pain                                       |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (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          |
| osteoarthritis                                  |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Infections and infestations                     |                |                 |                |
| acute hepatitis b                               |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| bronchitis                                      |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| gastroenteritis                                 |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (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          |
| gastroenteritis viral                           |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 1 / 61 (1.64%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| helicobacter gastritis                          |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| herpes simplex                                  |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| herpes zoster                                   |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 4 / 108 (3.70%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 3 / 4           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| pneumonia                                       |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| pneumonia bacterial                             |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 108 (0.00%) | 0 / 61 (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          |
| Metabolism and nutrition disorders              |                |                 |                |
| dehydration                                     |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 108 (0.93%) | 0 / 61 (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                                  |                |                 |                |
| alternative dictionary used: MedDRA 16.1        |                |                 |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 108 (0.00%) | 0 / 61 (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          |

|   |   |   |  |
|---|---|---|--|
| <b>Serious adverse events</b>                     | 4:8/4 mg LY3009104 once daily post-rescue Weeks 24-76 | 8/4 mg LY3009104 once daily Weeks 24-76 | 4/4 mg LY3009104 once daily Weeks 76-128 |
| Total subjects affected by serious adverse events |   |   |  |



|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed   | 6 / 61 (9.84%) | 6 / 32 (18.75%) | 5 / 79 (6.33%) |
| number of deaths (all causes)                                       | 0              | 1               | 0              |
| number of deaths resulting from adverse events                      | 0              | 0               | 0              |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                 |                |
| basal cell carcinoma  |                |                 |                |
| alternative dictionary used: MedDRA 16.1                            |                |                 |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%)  | 0 / 79 (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          |
| Pregnancy, puerperium and perinatal conditions                      |                |                 |                |
| abortion spontaneous  |                |                 |                |
| alternative dictionary used: MedDRA 16.1                            |                |                 |                |
| subjects affected / exposed <sup>[1]</sup>                          | 0 / 52 (0.00%) | 0 / 28 (0.00%)  | 0 / 62 (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          |
| pregnancy   |                |                 |                |
| alternative dictionary used: MedDRA 16.1                            |                |                 |                |
| subjects affected / exposed <sup>[2]</sup>                          | 1 / 52 (1.92%) | 0 / 28 (0.00%)  | 0 / 62 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0           | 0 / 0          |
| General disorders and administration site conditions                |                |                 |                |
| non-cardiac chest pain  |                |                 |                |
| alternative dictionary used: MedDRA 16.1                            |                |                 |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%)  | 1 / 79 (1.27%) |
| 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   |                |                 |                |
| alternative dictionary used: MedDRA 16.1                            |                |                 |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%)  | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0           | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders                     |                |                 |                |
| asthma  |                |                 |                |
| alternative dictionary used:  |                |                 |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| MedDRA 16.1                                     |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| pneumothorax                                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 32 (0.00%) | 0 / 79 (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                           |                |                |                |
| major depression                                |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| alanine aminotransferase increased              |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| aspartate aminotransferase increased            |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| blood creatine phosphokinase increased          |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| glomerular filtration rate decreased            |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| hepatic enzyme increased<br>alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| transaminases increased<br>alternative dictionary used:<br>MedDRA 16.1  |                |                |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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<br>alternative dictionary used:<br>MedDRA 16.1                     |                |                |                |
| subjects affected / exposed   | 1 / 61 (1.64%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| head injury<br>alternative dictionary used:<br>MedDRA 16.1              |                |                |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| jaw fracture<br>alternative dictionary used:<br>MedDRA 16.1             |                |                |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| rib fracture<br>alternative dictionary used:<br>MedDRA 16.1             |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| road traffic accident                           |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| scar  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| myocardial infarction                           |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 1 / 32 (3.13%) | 0 / 79 (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          |
| Nervous system disorders                        |                |                |                |
| carotid artery stenosis                         |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| presyncope                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 1 / 32 (3.13%) | 0 / 79 (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 dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| anaemia   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| microcytic anaemia                              |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| normochromic normocytic anaemia                 |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| pancytopenia                                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| cataract  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| ulcerative keratitis                            |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 61 (0.00%) | 1 / 32 (3.13%) | 0 / 79 (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          |
| Gastrointestinal disorders                      |                |                |                |
| coeliac disease                                 |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| colitis   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 1 / 32 (3.13%) | 0 / 79 (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          |
| gastritis                                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| large intestinal obstruction                    |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 1 / 79 (1.27%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| large intestinal stenosis                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 1 / 79 (1.27%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| cholecystitis                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| cholelithiasis                                  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 1 / 79 (1.27%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| angioedema                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| haematuria                                      |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| renal failure                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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 |                |                |                |
| arthritis                                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| diastasis recti abdominis                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 1 / 79 (1.27%) |
| occurrences causally related to treatment / all                               | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                                    | 0 / 0          | 0 / 0          | 0 / 0          |
| intervertebral disc protrusion<br>alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed   | 1 / 61 (1.64%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| neck pain<br>alternative dictionary used:<br>MedDRA 16.1                      |                |                |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| osteoarthritis<br>alternative dictionary used:<br>MedDRA 16.1                 |                |                |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 1 / 79 (1.27%) |
| occurrences causally related to treatment / all                               | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                                    | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations   |                |                |                |
| acute hepatitis b<br>alternative dictionary used:<br>MedDRA 16.1              |                |                |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 1 / 32 (3.13%) | 0 / 79 (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          |
| bronchitis<br>alternative dictionary used:<br>MedDRA 16.1                     |                |                |                |
| subjects affected / exposed   | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| gastroenteritis<br>alternative dictionary used:<br>MedDRA 16.1                |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| gastroenteritis viral                           |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |
| helicobacter gastritis                          |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| herpes simplex                                  |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 1 / 61 (1.64%) | 0 / 32 (0.00%) | 1 / 79 (1.27%) |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| herpes zoster                                   |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 1 / 32 (3.13%) | 1 / 79 (1.27%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pneumonia                                       |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| pneumonia bacterial                             |                |                |                |
| alternative dictionary used: MedDRA 16.1        |                |                |                |
| subjects affected / exposed                     | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (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          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Metabolism and nutrition disorders<br>dehydration<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed | 0 / 61 (0.00%) | 1 / 32 (3.13%) | 0 / 79 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| hyperglycaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed                                    | 0 / 61 (0.00%) | 0 / 32 (0.00%) | 0 / 79 (0.00%) |
| occurrences causally related to<br>treatment / all  | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>  | 4:8/4 mg<br>LY3009104 once<br>daily Weeks 76-128 | 8/4 mg LY3009104<br>once daily Weeks<br>76-128 | Follow-up       |
|--|--|--|-----------------|
| Total subjects affected by serious<br>adverse events   |  |  |                 |
| subjects affected / exposed  | 3 / 47 (6.38%)                                   | 0 / 18 (0.00%)                                 | 2 / 159 (1.26%) |
| number of deaths (all causes)  | 0  | 0  | 0               |
| number of deaths resulting from<br>adverse events  | 0  | 0  | 0               |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps)<br>basal cell carcinoma<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed | 0 / 47 (0.00%)                                   | 0 / 18 (0.00%)                                 | 0 / 159 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0  | 0 / 0  | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0  | 0 / 0  | 0 / 0           |
| Pregnancy, puerperium and perinatal<br>conditions<br>abortion spontaneous<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed <sup>[1]</sup>       | 0 / 40 (0.00%)                                   | 0 / 17 (0.00%)                                 | 1 / 130 (0.77%) |
| occurrences causally related to<br>treatment / all   | 0 / 0  | 0 / 0  | 0 / 1           |
| deaths causally related to<br>treatment / all  | 0 / 0  | 0 / 0  | 0 / 0           |
| pregnancy<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed <sup>[2]</sup>   | 0 / 40 (0.00%)                                   | 0 / 17 (0.00%)                                 | 0 / 130 (0.00%) |
| occurrences causally related to<br>treatment / all   | 0 / 0  | 0 / 0  | 0 / 0           |
| deaths causally related to<br>treatment / all  | 0 / 0  | 0 / 0  | 0 / 0           |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| General disorders and administration site conditions |                |                |                 |
| non-cardiac chest pain                               |                |                |                 |
| alternative dictionary used: MedDRA 16.1             |                |                |                 |
| subjects affected / exposed                          | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| pyrexia  |                |                |                 |
| alternative dictionary used: MedDRA 16.1             |                |                |                 |
| subjects affected / exposed                          | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders      |                |                |                 |
| asthma   |                |                |                 |
| alternative dictionary used: MedDRA 16.1             |                |                |                 |
| subjects affected / exposed                          | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| pneumothorax   |                |                |                 |
| alternative dictionary used: MedDRA 16.1             |                |                |                 |
| subjects affected / exposed                          | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Psychiatric disorders                                |                |                |                 |
| major depression                                     |                |                |                 |
| alternative dictionary used: MedDRA 16.1             |                |                |                 |
| subjects affected / exposed                          | 1 / 47 (2.13%) | 0 / 18 (0.00%) | 0 / 159 (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                                       |                |                |                 |
| alanine aminotransferase increased                   |                |                |                 |
| alternative dictionary used: MedDRA 16.1             |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| aspartate aminotransferase increased            |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| blood creatine phosphokinase increased          |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| glomerular filtration rate decreased            |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| hepatic enzyme increased                        |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 1 / 159 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| transaminases increased                         |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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 dictionary used: MedDRA 16.1        |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| head injury                                     |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| jaw fracture                                    |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| rib fracture                                    |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| road traffic accident                           |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| scar  |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Cardiac disorders                               |                |                |                 |
| myocardial infarction                           |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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                        |                |                |                 |
| carotid artery stenosis                         |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| presyncope                                      |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| syncope   |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 1 / 47 (2.13%) | 0 / 18 (0.00%) | 0 / 159 (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 dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| microcytic anaemia                              |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| normochromic normocytic anaemia                 |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| pancytopenia                                    |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Eye disorders                                   |                |                |                 |
| cataract  |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| ulcerative keratitis                            |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Gastrointestinal disorders                      |                |                |                 |
| coeliac disease                                 |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| colitis   |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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 dictionary used: MedDRA 16.1        |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed   | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| large intestinal obstruction<br>alternative dictionary used:<br>MedDRA 16.1 |                |                |                 |
| subjects affected / exposed   | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| large intestinal stenosis<br>alternative dictionary used:<br>MedDRA 16.1    |                |                |                 |
| subjects affected / exposed   | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0          | 0 / 0          | 0 / 0           |
| Hepatobiliary disorders   |                |                |                 |
| cholecystitis<br>alternative dictionary used:<br>MedDRA 16.1                |                |                |                 |
| subjects affected / exposed   | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| cholelithiasis<br>alternative dictionary used:<br>MedDRA 16.1               |                |                |                 |
| subjects affected / exposed   | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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                                      |                |                |                 |
| angioedema<br>alternative dictionary used:<br>MedDRA 16.1                   |                |                |                 |
| subjects affected / exposed   | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                                  | 0 / 0          | 0 / 0          | 0 / 0           |
| Renal and urinary disorders   |                |                |                 |
| haematuria<br>alternative dictionary used:<br>MedDRA 16.1                   |                |                |                 |



|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| renal failure                                   |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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 |                |                |                 |
| arthritis                                       |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| diastasis recti abdominis                       |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| intervertebral disc protrusion                  |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| neck pain                                       |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| osteoarthritis                                  |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Infections and infestations                     |                |                |                 |
| acute hepatitis b                               |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| bronchitis                                      |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| gastroenteritis                                 |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 1 / 47 (2.13%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| gastroenteritis viral                           |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| helicobacter gastritis                          |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| herpes simplex                                  |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| herpes zoster                                   |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| pneumonia                                       |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 2 / 47 (4.26%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| pneumonia bacterial                             |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| Metabolism and nutrition disorders              |                |                |                 |
| dehydration                                     |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 1 / 47 (2.13%) | 0 / 18 (0.00%) | 0 / 159 (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           |
| hyperglycaemia                                  |                |                |                 |
| alternative dictionary used: MedDRA 16.1        |                |                |                 |
| subjects affected / exposed                     | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (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           |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male or female subjects. The number of subjects exposed has been adjusted accordingly.

Frequency threshold for reporting non-serious adverse events: 4 %

| <b>Non-serious adverse events</b>                     | 1 mg LY3009104<br>once daily Weeks 0-<br>12 | 2 mg LY3009104<br>once daily Weeks 0-<br>12 | 4 mg LY3009104<br>once daily Weeks 0-<br>12 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events |   |   |   |
| subjects affected / exposed                           | 15 / 49 (30.61%)                            | 13 / 52 (25.00%)                            | 13 / 52 (25.00%)                            |
| Investigations  |   |   |   |
| alanine aminotransferase increased                    |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 0 / 49 (0.00%)                              | 1 / 52 (1.92%)                              | 0 / 52 (0.00%)                              |
| occurrences (all)                                     | 0   | 1   | 0   |
| blood cholesterol increased                           |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 2 / 49 (4.08%)                              | 1 / 52 (1.92%)                              | 2 / 52 (3.85%)                              |
| occurrences (all)                                     | 2   | 1   | 2   |
| blood creatine phosphokinase increased                |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 2 / 49 (4.08%)                              | 0 / 52 (0.00%)                              | 2 / 52 (3.85%)                              |
| occurrences (all)                                     | 2   | 0   | 2   |
| low density lipoprotein increased                     |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 0 / 49 (0.00%)                              | 0 / 52 (0.00%)                              | 1 / 52 (1.92%)                              |
| occurrences (all)                                     | 0   | 0   | 1   |
| weight increased                                      |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 0 / 49 (0.00%)                              | 0 / 52 (0.00%)                              | 0 / 52 (0.00%)                              |
| occurrences (all)                                     | 0   | 0   | 0   |
| Vascular disorders                                    |   |   |   |
| hypertension  |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 0 / 49 (0.00%)                              | 0 / 52 (0.00%)                              | 0 / 52 (0.00%)                              |
| occurrences (all)                                     | 0   | 0   | 0   |
| Surgical and medical procedures                       |   |   |   |

|   |   |   |   |
|---|---|---|---|
| spinal laminectomy<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 49 (0.00%)<br>0   | 0 / 52 (0.00%)<br>0   | 0 / 52 (0.00%)<br>0   |
| Nervous system disorders<br>dizziness<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>headache<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>syncope<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 49 (0.00%)<br>0<br><br>2 / 49 (4.08%)<br>2<br><br>0 / 49 (0.00%)<br>0 | 1 / 52 (1.92%)<br>1<br><br>1 / 52 (1.92%)<br>1<br><br>0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0<br><br>1 / 52 (1.92%)<br>1<br><br>0 / 52 (0.00%)<br>0 |
| Blood and lymphatic system disorders<br>anaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>leukopenia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>neutropenia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0<br><br>0 / 49 (0.00%)<br>0<br><br>0 / 49 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0 | 2 / 52 (3.85%)<br>2<br><br>0 / 52 (0.00%)<br>0<br><br>0 / 52 (0.00%)<br>0 |
| General disorders and administration<br>site conditions<br>oedema peripheral<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 2 / 49 (4.08%)<br>2   | 1 / 52 (1.92%)<br>1   | 0 / 52 (0.00%)<br>0   |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| pyrexia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 49 (2.04%)<br>1 | 0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 |
| Gastrointestinal disorders  |                     |                     |                     |
| abdominal discomfort<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)     | 0 / 49 (0.00%)<br>0 | 1 / 52 (1.92%)<br>1 | 0 / 52 (0.00%)<br>0 |
| abdominal pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)           | 0 / 49 (0.00%)<br>0 | 1 / 52 (1.92%)<br>1 | 0 / 52 (0.00%)<br>0 |
| acquired oesophageal web<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 |
| dyspepsia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                | 2 / 49 (4.08%)<br>2 | 0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 |
| gastritis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                | 0 / 49 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 |
| haemorrhoids<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)             | 0 / 49 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 |
| irritable bowel syndrome<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 |
| oesophagitis<br>alternative dictionary used:<br>MedDRA 16.1   |                     |                     |                     |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 49 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders   |                     |                     |                     |
| oropharyngeal pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0 | 1 / 52 (1.92%)<br>1 | 0 / 52 (0.00%)<br>0 |
| sinus congestion<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 49 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders  |                     |                     |                     |
| rash<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)               | 1 / 49 (2.04%)<br>1 | 1 / 52 (1.92%)<br>1 | 0 / 52 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders   |                     |                     |                     |
| back pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)          | 0 / 49 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 |
| Infections and infestations   |                     |                     |                     |
| bronchitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)         | 1 / 49 (2.04%)<br>1 | 1 / 52 (1.92%)<br>1 | 2 / 52 (3.85%)<br>2 |
| nasopharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)    | 0 / 49 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 | 2 / 52 (3.85%)<br>2 |
| pharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)        | 1 / 49 (2.04%)<br>1 | 1 / 52 (1.92%)<br>1 | 3 / 52 (5.77%)<br>3 |
| tooth abscess   |                     |                     |                     |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 49 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0 |
| upper respiratory tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 49 (0.00%)<br>0 | 1 / 52 (1.92%)<br>1 | 1 / 52 (1.92%)<br>1 |
| urinary tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                             | 2 / 49 (4.08%)<br>2 | 2 / 52 (3.85%)<br>2 | 2 / 52 (3.85%)<br>2 |
| Metabolism and nutrition disorders<br>dyslipidaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0 | 1 / 52 (1.92%)<br>1 | 0 / 52 (0.00%)<br>0 |
| hypercholesterolaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                               | 2 / 49 (4.08%)<br>2 | 2 / 52 (3.85%)<br>2 | 0 / 52 (0.00%)<br>0 |

| <b>Non-serious adverse events</b>   | 8 mg LY3009104<br>once daily Weeks 0-12 | Placebo once daily<br>Weeks 0-12 | 2 mg LY3009104<br>twice daily crossover<br>Weeks 12-24 |
|---|---|----------------------------------|--|
| Total subjects affected by non-serious adverse events   |   |                                  |  |
| subjects affected / exposed   | 15 / 50 (30.00%)                        | 18 / 98 (18.37%)                 | 15 / 63 (23.81%)                                       |
| Investigations  |   |                                  |  |
| alanine aminotransferase increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 1 / 50 (2.00%)<br>3                     | 3 / 98 (3.06%)<br>3              | 0 / 63 (0.00%)<br>0                                    |
| blood cholesterol increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)        | 2 / 50 (4.00%)<br>2                     | 2 / 98 (2.04%)<br>2              | 3 / 63 (4.76%)<br>3                                    |
| blood creatine phosphokinase increased<br>alternative dictionary used:  |   |                                  |  |



|   |                |                |                |
|---|----------------|----------------|----------------|
| MedDRA 16.1                                 |                |                |                |
| subjects affected / exposed                 | 1 / 50 (2.00%) | 1 / 98 (1.02%) | 1 / 63 (1.59%) |
| occurrences (all)                           | 1              | 1              | 1              |
| low density lipoprotein increased           |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed                 | 1 / 50 (2.00%) | 2 / 98 (2.04%) | 4 / 63 (6.35%) |
| occurrences (all)                           | 1              | 2              | 4              |
| weight increased                            |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed                 | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Vascular disorders                          |                |                |                |
| hypertension                                |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed                 | 0 / 50 (0.00%) | 1 / 98 (1.02%) | 0 / 63 (0.00%) |
| occurrences (all)                           | 0              | 1              | 0              |
| Surgical and medical procedures             |                |                |                |
| spinal laminectomy                          |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed                 | 0 / 50 (0.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0              |
| Nervous system disorders                    |                |                |                |
| dizziness                                   |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed                 | 1 / 50 (2.00%) | 0 / 98 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all)                           | 1              | 0              | 0              |
| headache                                    |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed                 | 2 / 50 (4.00%) | 2 / 98 (2.04%) | 2 / 63 (3.17%) |
| occurrences (all)                           | 3              | 2              | 2              |
| syncope                                     |                |                |                |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed                 | 0 / 50 (0.00%) | 1 / 98 (1.02%) | 0 / 63 (0.00%) |
| occurrences (all)                           | 0              | 1              | 0              |
| Blood and lymphatic system disorders        |                |                |                |

|  |  |  |  |
|--|--|--|--|
| <p>anaemia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 50 (0.00%)</p> <p>0</p>   | <p>0 / 98 (0.00%)</p> <p>0</p>   | <p>1 / 63 (1.59%)</p> <p>1</p>   |
| <p>leukopenia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>2 / 50 (4.00%)</p> <p>2</p>   | <p>0 / 98 (0.00%)</p> <p>0</p>   | <p>0 / 63 (0.00%)</p> <p>0</p>   |
| <p>neutropenia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 50 (0.00%)</p> <p>0</p>   | <p>0 / 98 (0.00%)</p> <p>0</p>   | <p>1 / 63 (1.59%)</p> <p>1</p>   |
| <p>General disorders and administration<br/>site conditions</p> <p>oedema peripheral</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pyrexia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 50 (0.00%)</p> <p>0</p> <p>0 / 50 (0.00%)</p> <p>0</p>                                | <p>0 / 98 (0.00%)</p> <p>0</p> <p>0 / 98 (0.00%)</p> <p>0</p>                                | <p>1 / 63 (1.59%)</p> <p>1</p> <p>0 / 63 (0.00%)</p> <p>0</p>                                |
| <p>Gastrointestinal disorders</p> <p>abdominal discomfort</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>abdominal pain</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>acquired oesophageal web</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dyspepsia</p> | <p>0 / 50 (0.00%)</p> <p>0</p> <p>0 / 50 (0.00%)</p> <p>0</p> <p>0 / 50 (0.00%)</p> <p>0</p> | <p>0 / 98 (0.00%)</p> <p>0</p> <p>0 / 98 (0.00%)</p> <p>0</p> <p>0 / 98 (0.00%)</p> <p>0</p> | <p>0 / 63 (0.00%)</p> <p>0</p> <p>0 / 63 (0.00%)</p> <p>0</p> <p>0 / 63 (0.00%)</p> <p>0</p> |

|  |                     |                     |                     |
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| alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 50 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0 | 0 / 63 (0.00%)<br>0 |
| gastritis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 50 (0.00%)<br>0 | 1 / 98 (1.02%)<br>1 | 0 / 63 (0.00%)<br>0 |
| haemorrhoids<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 50 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0 | 0 / 63 (0.00%)<br>0 |
| irritable bowel syndrome<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 50 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0 | 0 / 63 (0.00%)<br>0 |
| oesophagitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 50 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0 | 0 / 63 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders<br>oropharyngeal pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 50 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0 | 0 / 63 (0.00%)<br>0 |
| sinus congestion<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 50 (0.00%)<br>0 | 0 / 98 (0.00%)<br>0 | 0 / 63 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders<br>rash<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 50 (0.00%)<br>0 | 1 / 98 (1.02%)<br>1 | 0 / 63 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders  |                     |                     |                     |

|  |  |  |  |
|--|--|--|--|
| back pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 50 (0.00%)<br>0  | 0 / 98 (0.00%)<br>0  | 1 / 63 (1.59%)<br>1  |
| Infections and infestations<br>bronchitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>nasopharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>pharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>tooth abscess<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>upper respiratory tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>urinary tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | <br>1 / 50 (2.00%)<br>1<br><br>1 / 50 (2.00%)<br>1<br><br>0 / 50 (0.00%)<br>0<br><br>0 / 50 (0.00%)<br>0<br><br>1 / 50 (2.00%)<br>1<br><br>2 / 50 (4.00%)<br>2 | <br>3 / 98 (3.06%)<br>3<br><br>2 / 98 (2.04%)<br>3<br><br>0 / 98 (0.00%)<br>0<br><br>0 / 98 (0.00%)<br>0<br><br>2 / 98 (2.04%)<br>2<br><br>4 / 98 (4.08%)<br>4 | <br>1 / 63 (1.59%)<br>1<br><br>1 / 63 (1.59%)<br>1<br><br>0 / 63 (0.00%)<br>0<br><br>0 / 63 (0.00%)<br>0<br><br>2 / 63 (3.17%)<br>2<br><br>1 / 63 (1.59%)<br>1 |
| Metabolism and nutrition disorders<br>dyslipidaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>hypercholesterolaemia  | <br>1 / 50 (2.00%)<br>1  | <br>0 / 98 (0.00%)<br>0  | <br>0 / 63 (0.00%)<br>0  |

|   |                |                |                |
|---|----------------|----------------|----------------|
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                |
| subjects affected / exposed                 | 2 / 50 (4.00%) | 2 / 98 (2.04%) | 1 / 63 (1.59%) |
| occurrences (all)                           | 2              | 2              | 1              |

| <b>Non-serious adverse events</b>                     | 4 mg LY3009104<br>once daily crossover<br>Weeks 12-24 | 2 mg LY3009104<br>once daily Weeks<br>12-24 | 4 mg LY3009104<br>once daily Weeks<br>12-24 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events |   |   |   |
| subjects affected / exposed                           | 10 / 63 (15.87%)                                      | 12 / 51 (23.53%)                            | 10 / 50 (20.00%)                            |
| Investigations  |   |   |   |
| alanine aminotransferase increased                    |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 0 / 63 (0.00%)  | 1 / 51 (1.96%)                              | 1 / 50 (2.00%)                              |
| occurrences (all)                                     | 0   | 1   | 1   |
| blood cholesterol increased                           |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 1 / 63 (1.59%)  | 0 / 51 (0.00%)                              | 1 / 50 (2.00%)                              |
| occurrences (all)                                     | 1   | 0   | 1   |
| blood creatine phosphokinase increased                |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 0 / 63 (0.00%)  | 2 / 51 (3.92%)                              | 1 / 50 (2.00%)                              |
| occurrences (all)                                     | 0   | 2   | 1   |
| low density lipoprotein increased                     |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 1 / 63 (1.59%)  | 1 / 51 (1.96%)                              | 1 / 50 (2.00%)                              |
| occurrences (all)                                     | 1   | 1   | 1   |
| weight increased                                      |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 0 / 63 (0.00%)  | 0 / 51 (0.00%)                              | 0 / 50 (0.00%)                              |
| occurrences (all)                                     | 0   | 0   | 0   |
| Vascular disorders                                    |   |   |   |
| hypertension  |   |   |   |
| alternative dictionary used:<br>MedDRA 16.1           |   |   |   |
| subjects affected / exposed                           | 0 / 63 (0.00%)  | 1 / 51 (1.96%)                              | 4 / 50 (8.00%)                              |
| occurrences (all)                                     | 0   | 1   | 5   |
| Surgical and medical procedures                       |   |   |   |

|   |   |   |   |
|---|---|---|---|
| spinal laminectomy<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 63 (0.00%)<br>0   | 0 / 51 (0.00%)<br>0   | 0 / 50 (0.00%)<br>0   |
| Nervous system disorders<br>dizziness<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>headache<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>syncope<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 63 (0.00%)<br>0<br><br><br>1 / 63 (1.59%)<br>1<br><br>0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0<br><br>1 / 51 (1.96%)<br>1<br><br>0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0<br><br>0 / 50 (0.00%)<br>0<br><br>0 / 50 (0.00%)<br>0 |
| Blood and lymphatic system disorders<br>anaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>leukopenia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>neutropenia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 63 (0.00%)<br>0<br><br><br>0 / 63 (0.00%)<br>0<br><br>0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0<br><br>0 / 51 (0.00%)<br>0<br><br>0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0<br><br>0 / 50 (0.00%)<br>0<br><br>0 / 50 (0.00%)<br>0 |
| General disorders and administration<br>site conditions<br>oedema peripheral<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 63 (0.00%)<br>0   | 0 / 51 (0.00%)<br>0   | 1 / 50 (2.00%)<br>1   |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| pyrexia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Gastrointestinal disorders<br>abdominal discomfort<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| abdominal pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 63 (0.00%)<br>0 | 1 / 51 (1.96%)<br>1 | 0 / 50 (0.00%)<br>0 |
| acquired oesophageal web<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| dyspepsia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 1 / 63 (1.59%)<br>2 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| gastritis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 63 (0.00%)<br>0 | 1 / 51 (1.96%)<br>1 | 1 / 50 (2.00%)<br>1 |
| haemorrhoids<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| irritable bowel syndrome<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| oesophagitis<br>alternative dictionary used:<br>MedDRA 16.1   |                     |                     |                     |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders   |                     |                     |                     |
| oropharyngeal pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| sinus congestion<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 1 / 63 (1.59%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders  |                     |                     |                     |
| rash<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)               | 1 / 63 (1.59%)<br>1 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders   |                     |                     |                     |
| back pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)          | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Infections and infestations   |                     |                     |                     |
| bronchitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)         | 2 / 63 (3.17%)<br>2 | 2 / 51 (3.92%)<br>2 | 0 / 50 (0.00%)<br>0 |
| nasopharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)    | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| pharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)        | 0 / 63 (0.00%)<br>0 | 2 / 51 (3.92%)<br>2 | 0 / 50 (0.00%)<br>0 |
| tooth abscess   |                     |                     |                     |



|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| upper respiratory tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                   | 4 / 63 (6.35%)<br>4 | 2 / 51 (3.92%)<br>2 | 1 / 50 (2.00%)<br>1 |
| urinary tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 63 (1.59%)<br>1 | 2 / 51 (3.92%)<br>2 | 1 / 50 (2.00%)<br>1 |
| Metabolism and nutrition disorders<br>dyslipidaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| hypercholesterolaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 63 (0.00%)<br>0 | 0 / 51 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |

| <b>Non-serious adverse events</b>   | 8 mg LY3009104<br>once daily Weeks<br>12-24 | 4/4 mg LY3009104<br>once daily Weeks<br>24-76 | 4:8/4 mg<br>LY3009104 once<br>daily pre-rescue<br>Weeks 24-76 |
|---|---|---|---|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed   | 18 / 49 (36.73%)                            | 35 / 108 (32.41%)                             | 7 / 61 (11.48%)   |
| Investigations<br>alanine aminotransferase increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 1 / 49 (2.04%)<br>1                         | 1 / 108 (0.93%)<br>1                          | 0 / 61 (0.00%)<br>0   |
| blood cholesterol increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                          | 3 / 49 (6.12%)<br>4                         | 3 / 108 (2.78%)<br>4                          | 0 / 61 (0.00%)<br>0   |
| blood creatine phosphokinase<br>increased   |   |   |   |

|  |                     |                      |                     |
|--|---------------------|----------------------|---------------------|
| alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 2 / 49 (4.08%)<br>2 | 1 / 108 (0.93%)<br>1 | 1 / 61 (1.64%)<br>1 |
| low density lipoprotein increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 49 (6.12%)<br>3 | 0 / 108 (0.00%)<br>0 | 0 / 61 (0.00%)<br>0 |
| weight increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 49 (0.00%)<br>0 | 0 / 108 (0.00%)<br>0 | 0 / 61 (0.00%)<br>0 |
| Vascular disorders<br>hypertension<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 49 (2.04%)<br>1 | 1 / 108 (0.93%)<br>1 | 0 / 61 (0.00%)<br>0 |
| Surgical and medical procedures<br>spinal laminectomy<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0 | 0 / 108 (0.00%)<br>0 | 0 / 61 (0.00%)<br>0 |
| Nervous system disorders<br>dizziness<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 49 (0.00%)<br>0 | 1 / 108 (0.93%)<br>1 | 0 / 61 (0.00%)<br>0 |
| headache<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 49 (0.00%)<br>0 | 1 / 108 (0.93%)<br>1 | 1 / 61 (1.64%)<br>1 |
| syncope<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 49 (0.00%)<br>0 | 0 / 108 (0.00%)<br>0 | 0 / 61 (0.00%)<br>0 |
| Blood and lymphatic system disorders   |                     |                      |                     |

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|--|--|---|--|
| <p>anaemia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 49 (2.04%)</p> <p>1</p>   | <p>0 / 108 (0.00%)</p> <p>0</p>   | <p>1 / 61 (1.64%)</p> <p>1</p>   |
| <p>leukopenia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 49 (2.04%)</p> <p>1</p>   | <p>0 / 108 (0.00%)</p> <p>0</p>   | <p>0 / 61 (0.00%)</p> <p>0</p>   |
| <p>neutropenia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 49 (2.04%)</p> <p>1</p>   | <p>0 / 108 (0.00%)</p> <p>0</p>   | <p>0 / 61 (0.00%)</p> <p>0</p>   |
| <p>General disorders and administration site conditions</p> <p>oedema peripheral</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pyrexia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 49 (2.04%)</p> <p>1</p> <p>2 / 49 (4.08%)</p> <p>2</p>                                | <p>0 / 108 (0.00%)</p> <p>0</p> <p>0 / 108 (0.00%)</p> <p>0</p>                                 | <p>0 / 61 (0.00%)</p> <p>0</p> <p>0 / 61 (0.00%)</p> <p>0</p>                                |
| <p>Gastrointestinal disorders</p> <p>abdominal discomfort</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>abdominal pain</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>acquired oesophageal web</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dyspepsia</p> | <p>0 / 49 (0.00%)</p> <p>0</p> <p>1 / 49 (2.04%)</p> <p>1</p> <p>0 / 49 (0.00%)</p> <p>0</p> | <p>0 / 108 (0.00%)</p> <p>0</p> <p>0 / 108 (0.00%)</p> <p>0</p> <p>0 / 108 (0.00%)</p> <p>0</p> | <p>0 / 61 (0.00%)</p> <p>0</p> <p>0 / 61 (0.00%)</p> <p>0</p> <p>0 / 61 (0.00%)</p> <p>0</p> |

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|--|--------------------------------|---------------------------------|--------------------------------|
| <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 49 (2.04%)</p> <p>1</p> | <p>0 / 108 (0.00%)</p> <p>0</p> | <p>0 / 61 (0.00%)</p> <p>0</p> |
| <p>gastritis</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 49 (0.00%)</p> <p>0</p> | <p>1 / 108 (0.93%)</p> <p>1</p> | <p>0 / 61 (0.00%)</p> <p>0</p> |
| <p>haemorrhoids</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 49 (0.00%)</p> <p>0</p> | <p>0 / 108 (0.00%)</p> <p>0</p> | <p>0 / 61 (0.00%)</p> <p>0</p> |
| <p>irritable bowel syndrome</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 49 (0.00%)</p> <p>0</p> | <p>0 / 108 (0.00%)</p> <p>0</p> | <p>0 / 61 (0.00%)</p> <p>0</p> |
| <p>oesophagitis</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 49 (0.00%)</p> <p>0</p> | <p>0 / 108 (0.00%)</p> <p>0</p> | <p>0 / 61 (0.00%)</p> <p>0</p> |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>oropharyngeal pain</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 49 (4.08%)</p> <p>2</p> | <p>0 / 108 (0.00%)</p> <p>0</p> | <p>0 / 61 (0.00%)</p> <p>0</p> |
| <p>sinus congestion</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 49 (0.00%)</p> <p>0</p> | <p>0 / 108 (0.00%)</p> <p>0</p> | <p>0 / 61 (0.00%)</p> <p>0</p> |
| <p>Skin and subcutaneous tissue disorders</p> <p>rash</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                        | <p>0 / 49 (0.00%)</p> <p>0</p> | <p>0 / 108 (0.00%)</p> <p>0</p> | <p>1 / 61 (1.64%)</p> <p>1</p> |
| <p>Musculoskeletal and connective tissue disorders</p>   |                                |                                 |                                |

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| back pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 49 (0.00%)<br>0  | 1 / 108 (0.93%)<br>1   | 0 / 61 (0.00%)<br>0  |
| Infections and infestations<br>bronchitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>nasopharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>pharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>tooth abscess<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>upper respiratory tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>urinary tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0<br><br>2 / 49 (4.08%)<br>2<br><br>0 / 49 (0.00%)<br>0<br><br>0 / 49 (0.00%)<br>0<br><br>2 / 49 (4.08%)<br>2<br><br>2 / 49 (4.08%)<br>2 | 9 / 108 (8.33%)<br>9<br><br>2 / 108 (1.85%)<br>2<br><br>1 / 108 (0.93%)<br>1<br><br>0 / 108 (0.00%)<br>0<br><br>9 / 108 (8.33%)<br>10<br><br>12 / 108 (11.11%)<br>15 | 0 / 61 (0.00%)<br>0<br><br>0 / 61 (0.00%)<br>0<br><br>1 / 61 (1.64%)<br>1<br><br>0 / 61 (0.00%)<br>0<br><br>1 / 61 (1.64%)<br>1<br><br>1 / 61 (1.64%)<br>1 |
| Metabolism and nutrition disorders<br>dyslipidaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>hypercholesterolaemia  | 0 / 49 (0.00%)<br>0  | 0 / 108 (0.00%)<br>0   | 0 / 61 (0.00%)<br>0  |

|   |                         |                          |                         |
|---|-------------------------|--------------------------|-------------------------|
| alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 4 / 49 (8.16%)<br><br>4 | 1 / 108 (0.93%)<br><br>1 | 1 / 61 (1.64%)<br><br>1 |
|---|-------------------------|--------------------------|-------------------------|

| <b>Non-serious adverse events</b>  | 4:8/4 mg<br>LY3009104 once<br>daily post-rescue<br>Weeks 24-76 | 8/4 mg LY3009104<br>once daily Weeks<br>24-76 | 4/4 mg LY3009104<br>once daily Weeks<br>76-128 |
|--|--|---|--|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed  | 25 / 61 (40.98%)   | 16 / 32 (50.00%)                              | 24 / 79 (30.38%)                               |
| Investigations   |  |   |  |
| alanine aminotransferase increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)        | 0 / 61 (0.00%)<br><br>0  | 0 / 32 (0.00%)<br><br>0                       | 1 / 79 (1.27%)<br><br>1                        |
| blood cholesterol increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)               | 0 / 61 (0.00%)<br><br>0  | 0 / 32 (0.00%)<br><br>0                       | 4 / 79 (5.06%)<br><br>4                        |
| blood creatine phosphokinase<br>increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 2 / 61 (3.28%)<br><br>2  | 0 / 32 (0.00%)<br><br>0                       | 1 / 79 (1.27%)<br><br>1                        |
| low density lipoprotein increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)         | 0 / 61 (0.00%)<br><br>0  | 0 / 32 (0.00%)<br><br>0                       | 3 / 79 (3.80%)<br><br>3                        |
| weight increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                          | 3 / 61 (4.92%)<br><br>3  | 0 / 32 (0.00%)<br><br>0                       | 1 / 79 (1.27%)<br><br>1                        |
| Vascular disorders   |  |   |  |
| hypertension<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 61 (0.00%)<br><br>0  | 0 / 32 (0.00%)<br><br>0                       | 0 / 79 (0.00%)<br><br>0                        |
| Surgical and medical procedures  |  |   |  |

|   |   |   |   |
|---|---|---|---|
| spinal laminectomy<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 61 (0.00%)<br>0   | 0 / 32 (0.00%)<br>0   | 0 / 79 (0.00%)<br>0   |
| Nervous system disorders<br>dizziness<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>headache<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>syncope<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 61 (0.00%)<br>0<br><br>0 / 61 (0.00%)<br>0<br><br>0 / 61 (0.00%)<br>0 | 2 / 32 (6.25%)<br>2<br><br>0 / 32 (0.00%)<br>0<br><br>0 / 32 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0<br><br>0 / 79 (0.00%)<br>0<br><br>0 / 79 (0.00%)<br>0 |
| Blood and lymphatic system disorders<br>anaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>leukopenia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>neutropenia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 61 (0.00%)<br>0<br><br>0 / 61 (0.00%)<br>0<br><br>0 / 61 (0.00%)<br>0 | 2 / 32 (6.25%)<br>2<br><br>0 / 32 (0.00%)<br>0<br><br>1 / 32 (3.13%)<br>1 | 1 / 79 (1.27%)<br>1<br><br>0 / 79 (0.00%)<br>0<br><br>1 / 79 (1.27%)<br>1 |
| General disorders and administration<br>site conditions<br>oedema peripheral<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 1 / 61 (1.64%)<br>2   | 1 / 32 (3.13%)<br>1   | 0 / 79 (0.00%)<br>0   |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| pyrexia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 1 / 61 (1.64%)<br>1 | 0 / 32 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| Gastrointestinal disorders<br>abdominal discomfort<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 61 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| abdominal pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 61 (0.00%)<br>0 | 1 / 32 (3.13%)<br>1 | 0 / 79 (0.00%)<br>0 |
| acquired oesophageal web<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 61 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| dyspepsia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 1 / 61 (1.64%)<br>1 | 0 / 32 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| gastritis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 0 / 61 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| haemorrhoids<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 61 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| irritable bowel syndrome<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 61 (0.00%)<br>0 | 2 / 32 (6.25%)<br>2 | 0 / 79 (0.00%)<br>0 |
| oesophagitis<br>alternative dictionary used:<br>MedDRA 16.1   |                     |                     |                     |



|   |                     |                      |                     |
|---|---------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 61 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0  | 0 / 79 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders   |                     |                      |                     |
| oropharyngeal pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 0 / 61 (0.00%)<br>0 | 1 / 32 (3.13%)<br>1  | 0 / 79 (0.00%)<br>0 |
| sinus congestion<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 1 / 61 (1.64%)<br>1 | 0 / 32 (0.00%)<br>0  | 1 / 79 (1.27%)<br>1 |
| Skin and subcutaneous tissue disorders  |                     |                      |                     |
| rash<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)               | 0 / 61 (0.00%)<br>0 | 0 / 32 (0.00%)<br>0  | 1 / 79 (1.27%)<br>1 |
| Musculoskeletal and connective tissue disorders   |                     |                      |                     |
| back pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)          | 0 / 61 (0.00%)<br>0 | 2 / 32 (6.25%)<br>2  | 1 / 79 (1.27%)<br>1 |
| Infections and infestations   |                     |                      |                     |
| bronchitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)         | 3 / 61 (4.92%)<br>3 | 5 / 32 (15.63%)<br>5 | 3 / 79 (3.80%)<br>3 |
| nasopharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)    | 4 / 61 (6.56%)<br>4 | 1 / 32 (3.13%)<br>1  | 7 / 79 (8.86%)<br>9 |
| pharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)        | 1 / 61 (1.64%)<br>1 | 2 / 32 (6.25%)<br>3  | 2 / 79 (2.53%)<br>2 |
| tooth abscess   |                     |                      |                     |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)  | 1 / 61 (1.64%)<br>1 | 0 / 32 (0.00%)<br>0 | 0 / 79 (0.00%)<br>0 |
| upper respiratory tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                   | 6 / 61 (9.84%)<br>8 | 1 / 32 (3.13%)<br>1 | 3 / 79 (3.80%)<br>5 |
| urinary tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                             | 5 / 61 (8.20%)<br>6 | 3 / 32 (9.38%)<br>3 | 3 / 79 (3.80%)<br>4 |
| Metabolism and nutrition disorders<br>dyslipidaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 2 / 61 (3.28%)<br>2 | 2 / 32 (6.25%)<br>2 | 4 / 79 (5.06%)<br>4 |
| hypercholesterolaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 61 (1.64%)<br>1 | 0 / 32 (0.00%)<br>0 | 1 / 79 (1.27%)<br>1 |

| <b>Non-serious adverse events</b>   | 4:8/4 mg<br>LY3009104 once<br>daily Weeks 76-128 | 8/4 mg LY3009104<br>once daily Weeks<br>76-128 | Follow-up            |
|---|--|--|----------------------|
| Total subjects affected by non-serious adverse events   |  |  |                      |
| subjects affected / exposed   | 13 / 47 (27.66%)                                 | 10 / 18 (55.56%)                               | 5 / 159 (3.14%)      |
| Investigations  |  |  |                      |
| alanine aminotransferase increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | 3 / 47 (6.38%)<br>4                              | 0 / 18 (0.00%)<br>0                            | 0 / 159 (0.00%)<br>0 |
| blood cholesterol increased<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)        | 0 / 47 (0.00%)<br>0                              | 0 / 18 (0.00%)<br>0                            | 0 / 159 (0.00%)<br>0 |
| blood creatine phosphokinase increased<br>alternative dictionary used:  |  |  |                      |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| MedDRA 16.1                                 |                |                |                 |
| subjects affected / exposed                 | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0               |
| low density lipoprotein increased           |                |                |                 |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                 |
| subjects affected / exposed                 | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0               |
| weight increased                            |                |                |                 |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                 |
| subjects affected / exposed                 | 1 / 47 (2.13%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences (all)                           | 1              | 0              | 0               |
| Vascular disorders                          |                |                |                 |
| hypertension                                |                |                |                 |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                 |
| subjects affected / exposed                 | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0               |
| Surgical and medical procedures             |                |                |                 |
| spinal laminectomy                          |                |                |                 |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                 |
| subjects affected / exposed                 | 0 / 47 (0.00%) | 1 / 18 (5.56%) | 0 / 159 (0.00%) |
| occurrences (all)                           | 0              | 1              | 0               |
| Nervous system disorders                    |                |                |                 |
| dizziness                                   |                |                |                 |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                 |
| subjects affected / exposed                 | 1 / 47 (2.13%) | 1 / 18 (5.56%) | 0 / 159 (0.00%) |
| occurrences (all)                           | 1              | 1              | 0               |
| headache                                    |                |                |                 |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                 |
| subjects affected / exposed                 | 0 / 47 (0.00%) | 0 / 18 (0.00%) | 0 / 159 (0.00%) |
| occurrences (all)                           | 0              | 0              | 0               |
| syncope                                     |                |                |                 |
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                 |
| subjects affected / exposed                 | 0 / 47 (0.00%) | 1 / 18 (5.56%) | 0 / 159 (0.00%) |
| occurrences (all)                           | 0              | 1              | 0               |
| Blood and lymphatic system disorders        |                |                |                 |

|  |  |  |   |
|--|--|--|---|
| <p>anaemia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>1 / 47 (2.13%)</p> <p>1</p>   | <p>0 / 18 (0.00%)</p> <p>0</p>   | <p>0 / 159 (0.00%)</p> <p>0</p>   |
| <p>leukopenia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 47 (0.00%)</p> <p>0</p>   | <p>1 / 18 (5.56%)</p> <p>2</p>   | <p>0 / 159 (0.00%)</p> <p>0</p>   |
| <p>neutropenia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 47 (0.00%)</p> <p>0</p>   | <p>1 / 18 (5.56%)</p> <p>1</p>   | <p>0 / 159 (0.00%)</p> <p>0</p>   |
| <p>General disorders and administration<br/>site conditions</p> <p>oedema peripheral</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>pyrexia</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 47 (2.13%)</p> <p>1</p> <p>0 / 47 (0.00%)</p> <p>0</p>                                | <p>0 / 18 (0.00%)</p> <p>0</p> <p>0 / 18 (0.00%)</p> <p>0</p>                                | <p>1 / 159 (0.63%)</p> <p>1</p> <p>0 / 159 (0.00%)</p> <p>0</p>                                 |
| <p>Gastrointestinal disorders</p> <p>abdominal discomfort</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>abdominal pain</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>acquired oesophageal web</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>dyspepsia</p> | <p>0 / 47 (0.00%)</p> <p>0</p> <p>1 / 47 (2.13%)</p> <p>1</p> <p>0 / 47 (0.00%)</p> <p>0</p> | <p>1 / 18 (5.56%)</p> <p>1</p> <p>1 / 18 (5.56%)</p> <p>1</p> <p>1 / 18 (5.56%)</p> <p>1</p> | <p>0 / 159 (0.00%)</p> <p>0</p> <p>0 / 159 (0.00%)</p> <p>0</p> <p>0 / 159 (0.00%)</p> <p>0</p> |

|  |                                |                                |                                 |
|--|--------------------------------|--------------------------------|---------------------------------|
| <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 47 (0.00%)</p> <p>0</p> | <p>0 / 18 (0.00%)</p> <p>0</p> | <p>0 / 159 (0.00%)</p> <p>0</p> |
| <p>gastritis</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 47 (0.00%)</p> <p>0</p> | <p>1 / 18 (5.56%)</p> <p>1</p> | <p>0 / 159 (0.00%)</p> <p>0</p> |
| <p>haemorrhoids</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>1 / 47 (2.13%)</p> <p>1</p> | <p>1 / 18 (5.56%)</p> <p>1</p> | <p>0 / 159 (0.00%)</p> <p>0</p> |
| <p>irritable bowel syndrome</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 47 (0.00%)</p> <p>0</p> | <p>0 / 18 (0.00%)</p> <p>0</p> | <p>0 / 159 (0.00%)</p> <p>0</p> |
| <p>oesophagitis</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 47 (0.00%)</p> <p>0</p> | <p>1 / 18 (5.56%)</p> <p>1</p> | <p>0 / 159 (0.00%)</p> <p>0</p> |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>oropharyngeal pain</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 47 (0.00%)</p> <p>0</p> | <p>0 / 18 (0.00%)</p> <p>0</p> | <p>0 / 159 (0.00%)</p> <p>0</p> |
| <p>sinus congestion</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 47 (0.00%)</p> <p>0</p> | <p>1 / 18 (5.56%)</p> <p>1</p> | <p>0 / 159 (0.00%)</p> <p>0</p> |
| <p>Skin and subcutaneous tissue disorders</p> <p>rash</p> <p>alternative dictionary used:<br/>MedDRA 16.1</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                        | <p>0 / 47 (0.00%)</p> <p>0</p> | <p>1 / 18 (5.56%)</p> <p>1</p> | <p>1 / 159 (0.63%)</p> <p>1</p> |
| <p>Musculoskeletal and connective tissue disorders</p>   |                                |                                |                                 |

|  |  |   |  |
|--|--|---|--|
| back pain<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)   | 0 / 47 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1   | 0 / 159 (0.00%)<br>0   |
| Infections and infestations<br>bronchitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>nasopharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>pharyngitis<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>tooth abscess<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>upper respiratory tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>urinary tract infection<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all) | <br>2 / 47 (4.26%)<br>2<br><br>2 / 47 (4.26%)<br>2<br><br>1 / 47 (2.13%)<br>1<br><br>1 / 47 (2.13%)<br>1<br><br>2 / 47 (4.26%)<br>3<br><br>1 / 47 (2.13%)<br>1 | <br>1 / 18 (5.56%)<br>1<br><br>2 / 18 (11.11%)<br>3<br><br>0 / 18 (0.00%)<br>0<br><br>1 / 18 (5.56%)<br>1<br><br>1 / 18 (5.56%)<br>1<br><br>0 / 18 (0.00%)<br>0 | <br>1 / 159 (0.63%)<br>1<br><br>0 / 159 (0.00%)<br>0<br><br>0 / 159 (0.00%)<br>0<br><br>0 / 159 (0.00%)<br>0<br><br>0 / 159 (0.00%)<br>0<br><br>2 / 159 (1.26%)<br>2 |
| Metabolism and nutrition disorders<br>dyslipidaemia<br>alternative dictionary used:<br>MedDRA 16.1<br>subjects affected / exposed<br>occurrences (all)<br><br>hypercholesterolaemia  | <br>0 / 47 (0.00%)<br>0  | <br>0 / 18 (0.00%)<br>0   | <br>0 / 159 (0.00%)<br>0   |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| alternative dictionary used:<br>MedDRA 16.1 |                |                |                 |
| subjects affected / exposed                 | 0 / 47 (0.00%) | 1 / 18 (5.56%) | 0 / 159 (0.00%) |
| occurrences (all)                           | 0              | 1              | 0               |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment  |
|--------------|--|
| 23 May 2011  | <p>Amendment I4V-MC-JADA(a): An open-label extension period (referred to as Part C of the study) was added as an optional extension of the study for patients who completed 24 weeks of treatment and met enrollment criteria. The open-label extension period was added to collect additional safety data, and to examine the effect of long-term administration of LY3009104 on efficacy measures.</p> <ul style="list-style-type: none"><li>o New secondary and exploratory objectives were added to evaluate the safety and tolerability of long-term administration of LY3009104, and to examine the effects of long-term administration of LY3009104 on patient-reported outcomes.</li><li>o Blinding information was clarified throughout the document to distinguish the double-blind period (Part A and Part B) and the open-label extension period (Part C).</li><li>o Additional inclusion and exclusion criteria applicable to Part C of the study were added. Inclusion and exclusion criteria for Parts A and B were revised.</li><li>o Study design for Part C was provided. Study design for Parts A and B was updated.</li><li>o Use of concomitant medications during Part C of the study was added.</li><li>o The study schedule (Attachment 1 of the protocol amendment) of Parts A and B was updated. A study schedule was added to include assessments of Part C of the study.</li><li>o Treatment assignment for Part C of the study and dose escalation process during the open-label extension period were added.</li></ul> |
| 29 June 2012 | <p>Amendment I4V-MC-JADA(b) - An additional open-label extension period (referred to as Part D of the study) was added as an optional extension of the study for patients who completed 76 weeks of treatment and met enrollment criteria. This additional extension would allow for further evaluation of longer-term administration in patients who may have been receiving therapeutic benefit of 4 mg LY3009104 once daily and assist in characterization of the safety and tolerability profile of LY3009104. All patients who entered Part D would receive 4 mg LY3009104 once daily.</p> <ul style="list-style-type: none"><li>o Secondary and exploratory objectives were updated to reflect the addition of Part D.</li><li>o Blinding information was updated to reflect the addition of Part D.</li><li>o Additional inclusion and exclusion criteria applicable to Part D of the study were added.</li><li>o Study design for Part D was provided.</li><li>o Use of concomitant medications was updated to reflect the addition of Part D of the study.</li><li>o A study schedule was added to include assessments of Part D of the study.</li><li>o Treatment assignment for Part D of the study was added.</li><li>• Statistical methods were revised to reflect the addition of Part D.</li><li>• In general, changes were made to clarify study procedures and to keep consistency throughout the protocol.</li><li>• Editorial revisions with no impact on protocol design or implementation also were made.</li></ul>             |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats



None reported