



## Clinical trial results:

### A Randomized, Double-Blind, Multi-Center Study to Evaluate the Efficacy and Safety of Oral Solithromycin (CEM-101) Compared to Oral Moxifloxacin in the Treatment of Adult Patients with Community-Acquired Bacterial Pneumonia

#### Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2012-003971-20          |
| Trial protocol           | HU CZ ES PL LV EE BG RO |
| Global end of trial date | 23 October 2014         |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 23 April 2016 |
| First version publication date | 23 April 2016 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | CE01-300 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01756339 |
| WHO universal trial number (UTN)   | -           |
| Other trial identifiers            | IND: 101317 |

Notes:

##### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Cempra Pharmaceuticals, Inc.   |
| Sponsor organisation address | 6320 Quadrangle Drive, Suite 360, Chapel Hill, United States, NC 27517       |
| Public contact               | Clinical Trials Info, Cempra Pharmaceuticals, Inc, clinicaltrials@cempra.com |
| Scientific contact           | Clinical Trials Info, Cempra Pharmaceuticals, Inc, clinicaltrials@cempra.com |

Notes:

##### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 05 February 2016 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 23 October 2014  |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 23 October 2014  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To determine the noninferiority (NI) oral solithromycin compared with oral moxifloxacin with respect to the following EMA co-primary endpoints: clinical response assessed at Test of Cure (TOC), also called Short-term Follow-Up Visit (SFU), 5-10 days after the last dose of study drug, in the Intent to Treat (ITT) population and clinically evaluable (CE-SFU) population.

Protection of trial subjects:

This study was conducted in compliance with the protocol and all regulatory requirements, in accordance with GCP, including International Conference on Harmonisation (ICH) guidelines, and in general conformity with the most recent version of the Declaration of Helsinki.

Background therapy:

A single dose of a short-acting antibiotic (penicillins, cephalosporins [not ceftriaxone], tetracyclines, or trimethoprim-sulfamethoxazole) in the 7 days prior to enrolment was permitted (number of patient limited to 25% of the population).

Evidence for comparator:

Moxifloxacin was chosen as the active comparator for multiple reasons.

It has established efficacy in the treatment of CABP, with potent activity against key pathogens associated with CABP. Moxifloxacin is recommended empiric therapy for moderately severe CABP in the EU and USA. Additionally, moxifloxacin is available in IV and oral formulations, and thus is an appropriate comparator for both this study and Study CE01-301, the Phase 3 solithromycin IV-to-Oral CABP trial. It was also possible to define a common moxifloxacin regimen for all countries in which the study was conducted.

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 03 January 2013 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | Yes             |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Poland: 29         |
| Country: Number of subjects enrolled | Romania: 106       |
| Country: Number of subjects enrolled | Spain: 16          |
| Country: Number of subjects enrolled | Bulgaria: 67       |
| Country: Number of subjects enrolled | Czech Republic: 11 |
| Country: Number of subjects enrolled | Estonia: 2         |
| Country: Number of subjects enrolled | Germany: 2         |
| Country: Number of subjects enrolled | Hungary: 60        |
| Country: Number of subjects enrolled | Latvia: 9          |
| Country: Number of subjects enrolled | Argentina: 58      |

|                                      |                         |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Canada: 14              |
| Country: Number of subjects enrolled | Dominican Republic: 14  |
| Country: Number of subjects enrolled | Ecuador: 34             |
| Country: Number of subjects enrolled | Russian Federation: 146 |
| Country: Number of subjects enrolled | South Africa: 102       |
| Country: Number of subjects enrolled | United States: 190      |
| Worldwide total number of subjects   | 860                     |
| EEA total number of subjects         | 302                     |

Notes:

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### Subjects enrolled per age group

|   |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 568 |
| From 65 to 84 years                       | 281 |
| 85 years and over                         | 11  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 860 patients were enrolled from 114 centers in Europe (448 patients), North America (224 patients), Latin America (106 patients), and South Africa (102 patients). The first patient was enrolled 03 January 2013, the last patient was enrolled 25 September 2014, and the final study visit was conducted 23 October 2014.

### Pre-assignment

Screening details:

Eligible patients were males or females  $\geq 18$  years of age with an acute onset or worsening of at least 3 of the following signs and symptoms of CABP: cough, production of purulent sputum, shortness of breath (dyspnea), chest pain.

And at least 1 of the following: fever, hypothermia, presence of pulmonary rales and/or pulmonary consolidation.

### Period 1

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

Blinding implementation details:

A double-dummy design was utilized, with solithromycin placebo capsules identical in appearance to solithromycin capsules and moxifloxacin placebo over-encapsulated tablets identical in appearance to moxifloxacin overencapsulated tablets. All personnel involved with the evaluation of patient efficacy and safety were blind with the exception of an unblinded statistician who was responsible for generating tables for the Data Monitoring Committee (DMC) and the bioanalytical personnel.

### Arms

|                              |               |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes           |
| <b>Arm title</b>             | Solithromycin |

Arm description:

Solithromycin treatment group

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Solithromycin |
| Investigational medicinal product code | CEM-101       |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule, hard |
| Routes of administration               | Oral use      |

Dosage and administration details:

Day 1: Oral solithromycin 800 mg (4×200 mg capsules) and 1 oral moxifloxacin placebo capsule.

Days 2-5: Oral solithromycin 400 mg (2×200 mg capsules) and 1 oral moxifloxacin placebo capsule daily

Days 6-7: 2 Oral solithromycin placebo capsules and 1 oral moxifloxacin placebo capsule daily

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | Moxifloxacin |
|------------------|--------------|

Arm description:

Moxifloxacin treatment group

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Moxifloxacin      |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Tablet            |
| Routes of administration               | Oral use          |

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**Dosage and administration details:**

Day 1: Oral moxifloxacin 400 mg (1×400 mg over-encapsulated tablet) and 4 oral solithromycin placebo capsules

Days 2-7: Oral moxifloxacin 400 mg (1×400 mg over-encapsulated tablet) and 2 oral solithromycin placebo capsules daily

| <b>Number of subjects in period 1</b> | Solithromycin | Moxifloxacin |
|---------------------------------------|---------------|--------------|
| Started                               | 426           | 434          |
| Completed                             | 406           | 413          |
| Not completed                         | 20            | 21           |
| Adverse event, serious fatal          | 6             | 6            |
| Consent withdrawn by subject          | 11            | 6            |
| Physician decision                    | -             | 1            |
| Adverse event, non-fatal              | 1             | 2            |
| randomised in error                   | -             | 1            |
| Lost to follow-up                     | 2             | 5            |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Solithromycin |
|-----------------------|---------------|

Reporting group description:

Solithromycin treatment group

|                       |              |
|-----------------------|--------------|
| Reporting group title | Moxifloxacin |
|-----------------------|--------------|

Reporting group description:

Moxifloxacin treatment group

| Reporting group values                             | Solithromycin | Moxifloxacin | Total |
|--|---------------|--------------|-------|
| Number of subjects                                 | 426           | 434          | 860   |
| Age categorical                                    |               |              |       |
| Units: Subjects                                    |               |              |       |
| In utero   | 0             | 0            | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0             | 0            | 0     |
| Newborns (0-27 days)                               | 0             | 0            | 0     |
| Infants and toddlers (28 days-23 months)           | 0             | 0            | 0     |
| Children (2-11 years)                              | 0             | 0            | 0     |
| Adolescents (12-17 years)                          | 0             | 0            | 0     |
| Adults (18-64 years)                               | 271           | 297          | 568   |
| From 65-84 years                                   | 150           | 131          | 281   |
| 85 years and over                                  | 5             | 6            | 11    |
| Age continuous                                     |               |              |       |
| Units: years                                       |               |              |       |
| arithmetic mean                                    | 58.5          | 56.7         |       |
| standard deviation                                 | ± 14.7        | ± 15.5       | -     |
| Gender categorical                                 |               |              |       |
| Units: Subjects                                    |               |              |       |
| Female   | 199           | 205          | 404   |
| Male   | 227           | 229          | 456   |
| PORT risk class                                    |               |              |       |
| PORT core reported in the eCRF                     |               |              |       |
| Units: Subjects                                    |               |              |       |
| Port I   | 1             | 0            | 1     |
| Port II  | 209           | 223          | 432   |
| Port III   | 168           | 173          | 341   |
| Port IV  | 48            | 38           | 86    |

## End points

### End points reporting groups

|   |  |
|---|--|
| Reporting group title   | Solithromycin                            |
| Reporting group description:  |  |
| Solithromycin treatment group   |  |
| Reporting group title   | Moxifloxacin                             |
| Reporting group description:  |  |
| Moxifloxacin treatment group  |  |
| Subject analysis set title  | Solithromycin -ITT Set                   |
| Subject analysis set type   | Intention-to-treat                       |
| Subject analysis set description:   |  |
| The analysis set consists of all randomized patients regardless of whether or not the patient received study drug. A patient is considered randomized when the Investigator or Investigator's designee receives the IWRS-generated randomization number.  |  |
| Subject analysis set title  | Moxifloxacin - ITT Set                   |
| Subject analysis set type   | Intention-to-treat                       |
| Subject analysis set description:   |  |
| The ITT set consists of all randomized patients regardless of whether or not the patient received study drug. A patient is considered randomized when the Investigator or Investigator's designee receives the IWRS-generated randomization number.   |  |
| Subject analysis set title  | Solithromycin - Clinically Evaluable Set |
| Subject analysis set type   | Per protocol                             |
| Subject analysis set description:   |  |
| The Clinically Evaluable (CE) populations will consist of all patients in the ITT population who also meet the criteria listed in the SAP, among them: met key inclusion criteria, did not meet the exclusion criteria, completed the TOC Visit 5-10 days after the last dose of study drug, Received $\geq 2$ doses of study drug during the first 48 hours if the patient is a clinical failure, received $\geq 3$ doses of study drug during the first 72 hours if the patient is a clinical success, did not receive another systemic antibacterial from the first dose of study drug through EOT (end of treatment ) or through TOC with likely or documented activity against confirmed or potential CABP pathogens, received the correct study drug based on randomization assignment. |  |
| Subject analysis set title  | Moxifloxacin- Clinically Evaluable Set   |
| Subject analysis set type   | Per protocol                             |
| Subject analysis set description:   |  |
| The Clinically Evaluable (CE) populations will consist of all patients in the ITT population who also meet the criteria listed in the SAP, among them: met key inclusion criteria, did not meet the exclusion criteria, completed the TOC Visit 5-10 days after the last dose of study drug, Received $\geq 2$ doses of study drug during the first 48 hours if the patient is a clinical failure, received $\geq 3$ doses of study drug during the first 72 hours if the patient is a clinical success, did not receive another systemic antibacterial from the first dose of study drug through EOT (end of treatment ) or through TOC with likely or documented activity against confirmed or potential CABP pathogens, received the correct study drug based on randomization assignment. |  |

### Primary: Clinical response-ITT at TOC: non-inferiority hypothesis

|  |  |
|--|--|
| End point title  | Clinical response-ITT at TOC: non-inferiority hypothesis |
| End point description:   |  |
| Proportion of patients with clinical success of CABP symptoms.   |  |
| Clinical response rates at the TOC visit (or SFU visit) for the ITT Population is a co-primary endpoint of the study.                    |  |
| Clinical response (Investigator assessment) is classified as success, failure, or indeterminate according to the definitions in the SAP. |  |
| End point type   | Primary  |
| End point timeframe:   |  |
| At Test of Cure (TOC) , i.e. 5-10 days after last dose of study drug.  |  |

| <b>End point values</b>       | Solithromycin      | Moxifloxacin       |  |  |
|-------------------------------|--------------------|--------------------|--|--|
| Subject group type            | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed   | 426 <sup>[1]</sup> | 434 <sup>[2]</sup> |  |  |
| Units: number of patients (%) |                    |                    |  |  |
| success                       | 360                | 376                |  |  |
| failure                       | 49                 | 38                 |  |  |
| indeterminate                 | 17                 | 20                 |  |  |

Notes:

[1] - ITT Population

[2] - ITT Population

## Statistical analyses

| <b>Statistical analysis title</b>  | Non-inferiority hypothesis test (success)-ITT |
|--|---|
| Statistical analysis description:  |   |
| H0: Difference (Solithromycin treatment group minus Moxifloxacin treatment group) of clinical success rates $\leq -10\%$ |   |
| Comparison groups  | Solithromycin v Moxifloxacin                  |
| Number of subjects included in analysis  | 860   |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | non-inferiority <sup>[3]</sup>                |
| Parameter estimate   | Difference of clinical success rates          |
| Point estimate   | -2.13   |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | -6.9  |
| upper limit  | 2.6   |

Notes:

[3] - A non-inferiority margin of 10% was used.

## Primary: Clinical response- CE at TOC: non-inferiority hypothesis

| <b>End point title</b>  | Clinical response- CE at TOC: non-inferiority hypothesis |
|---|--|
| End point description:  |  |
| Proportion of patients with clinical success of CABP symptoms at TOC for the Clinically Evaluable (CE) Population is a co-primary endpoint. |  |
| Clinical response (Investigator assessment) is classified as success, failure or indeterminate according to the definition in the SAP.      |  |
| End point type  | Primary  |
| End point timeframe:  |  |
| At TOC  |  |



| <b>End point values</b>       | Solithromycin      | Moxifloxacin       |  |  |
|-------------------------------|--------------------|--------------------|--|--|
| Subject group type            | Reporting group    | Reporting group    |  |  |
| Number of subjects analysed   | 388 <sup>[4]</sup> | 390 <sup>[5]</sup> |  |  |
| Units: number of patients (%) |                    |                    |  |  |
| Success                       | 342                | 356                |  |  |
| Failure                       | 46                 | 33                 |  |  |
| Indeterminate                 | 0                  | 1                  |  |  |

Notes:

[4] - Clinically Evaluable Population

[5] - Clinically Evaluable Population

## Statistical analyses

| <b>Statistical analysis title</b>  | Non-inferiority hypothesis test (success) - CE |
|--|--|
| Statistical analysis description:  |  |
| H0: Difference (solithromycin minus Moxifloxacin treatment group) of clinical success rates $\leq$ -10%. |  |
| Comparison groups  | Solithromycin v Moxifloxacin                   |
| Number of subjects included in analysis  | 778  |
| Analysis specification   | Pre-specified                                  |
| Analysis type  | non-inferiority <sup>[6]</sup>                 |
| Parameter estimate   | Difference in clinical success rates           |
| Point estimate   | -3.14  |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided  |
| lower limit  | -7.6   |
| upper limit  | 1.1  |

Notes:

[6] - A non-inferiority margin of 10% was used.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first study drug administration to late follow-up visit (Day 28-35 after first dose of study drug).

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Solithromycin |
|-----------------------|---------------|

Reporting group description: -

|                       |              |
|-----------------------|--------------|
| Reporting group title | Moxifloxacin |
|-----------------------|--------------|

Reporting group description: -

| Serious adverse events  | Solithromycin    | Moxifloxacin     |  |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events                   |                  |                  |  |
| subjects affected / exposed   | 28 / 424 (6.60%) | 27 / 432 (6.25%) |  |
| number of deaths (all causes)                                       | 6                | 6                |  |
| number of deaths resulting from adverse events                      | 0                | 0                |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                  |                  |  |
| Leukaemia   |                  |                  |  |
| subjects affected / exposed   | 0 / 424 (0.00%)  | 1 / 432 (0.23%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            |  |
| Lung cancer metastatic  |                  |                  |  |
| subjects affected / exposed   | 1 / 424 (0.24%)  | 0 / 432 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            |  |
| Lung carcinoma cell type unspecified stage IV                       |                  |                  |  |
| subjects affected / exposed   | 0 / 424 (0.00%)  | 1 / 432 (0.23%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all                          | 0 / 0            | 0 / 0            |  |
| Lung neoplasm malignant   |                  |                  |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 424 (0.00%) | 2 / 432 (0.46%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Vascular disorders                                   |                 |                 |  |
| Deep vein thrombosis                                 |                 |                 |  |
| subjects affected / exposed                          | 1 / 424 (0.24%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Pregnancy, puerperium and perinatal conditions       |                 |                 |  |
| Pregnancy  |                 |                 |  |
| subjects affected / exposed                          | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Multi-organ failure                                  |                 |                 |  |
| subjects affected / exposed                          | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           |  |
| Respiratory, thoracic and mediastinal disorders      |                 |                 |  |
| Acute respiratory distress syndrome                  |                 |                 |  |
| subjects affected / exposed                          | 0 / 424 (0.00%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1           |  |
| Acute respiratory failure                            |                 |                 |  |
| subjects affected / exposed                          | 1 / 424 (0.24%) | 2 / 432 (0.46%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 2           |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0           |  |
| Asthma   |                 |                 |  |
| subjects affected / exposed                          | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Bronchitis chronic                                   |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Bronchospasm                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Chronic obstructive pulmonary disease           |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Hypoxia   |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pleural effusion                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pulmonary embolism                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Respiratory failure                             |                 |                 |  |
| subjects affected / exposed                     | 2 / 424 (0.47%) | 2 / 432 (0.46%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 2           |  |
| Injury, poisoning and procedural complications  |                 |                 |  |
| Femur fracture                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 424 (0.00%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Cardiac disorders                               |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Acute myocardial infarction                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0           |  |
| Atrial fibrillation                             |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| cardiac failure                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Cardiac failure congestive                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 424 (0.00%) | 2 / 432 (0.46%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Ventricular failure                             |                 |                 |  |
| subjects affected / exposed                     | 0 / 424 (0.00%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Nervous system disorders                        |                 |                 |  |
| Cerebrovascular accident                        |                 |                 |  |
| subjects affected / exposed                     | 2 / 424 (0.47%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 2           | 0 / 0           |  |
| Gastrointestinal disorders                      |                 |                 |  |
| Gastritis erosive                               |                 |                 |  |
| subjects affected / exposed                     | 0 / 424 (0.00%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Oesophageal obstruction                         |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Hepatobiliary disorders                         |                 |                 |  |
| Hepatorenal syndrome                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 424 (0.00%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| Renal and urinary disorders                     |                 |                 |  |
| Renal failure                                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Endocrine disorders                             |                 |                 |  |
| Thyroiditis subacute                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 424 (0.00%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infections and infestations                     |                 |                 |  |
| Empyema   |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Infectious pleural effusion                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Lung abscess                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 424 (0.00%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia                                       |                 |                 |  |
| subjects affected / exposed                     | 6 / 424 (1.42%) | 3 / 432 (0.69%) |  |
| occurrences causally related to treatment / all | 0 / 6           | 0 / 3           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia influenzal                            |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pneumonia pseudomonal                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Pulmonary tuberculosis                          |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 1 / 432 (0.23%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| Septic shock                                    |                 |                 |  |
| subjects affected / exposed                     | 1 / 424 (0.24%) | 0 / 432 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |

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

| <b>Non-serious adverse events</b>                     | Solithromycin     | Moxifloxacin      |  |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                   |                   |  |
| subjects affected / exposed                           | 65 / 424 (15.33%) | 62 / 432 (14.35%) |  |
| Nervous system disorders                              |                   |                   |  |
| Dizziness   |                   |                   |  |
| subjects affected / exposed                           | 9 / 424 (2.12%)   | 7 / 432 (1.62%)   |  |
| occurrences (all)                                     | 9                 | 7                 |  |
| Headache  |                   |                   |  |
| subjects affected / exposed                           | 19 / 424 (4.48%)  | 10 / 432 (2.31%)  |  |
| occurrences (all)                                     | 19                | 10                |  |
| Gastrointestinal disorders                            |                   |                   |  |
| Diarrhoea   |                   |                   |  |
| subjects affected / exposed                           | 15 / 424 (3.54%)  | 27 / 432 (6.25%)  |  |
| occurrences (all)                                     | 15                | 28                |  |
| Nausea  |                   |                   |  |
| subjects affected / exposed                           | 13 / 424 (3.07%)  | 16 / 432 (3.70%)  |  |
| occurrences (all)                                     | 13                | 16                |  |

|  |                      |                       |  |
|--|----------------------|-----------------------|--|
| Vomiting<br>subjects affected / exposed<br>occurrences (all) | 9 / 424 (2.12%)<br>9 | 9 / 432 (2.08%)<br>11 |  |
|--|----------------------|-----------------------|--|



## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported