

**Clinical trial results:****An Open Label, Randomized, Single Dose, Parallel Arm Study To Determine Pharmacokinetics Of Azithromycin Following Oral Administration Of Immediate-Release (IR) Or Extended-Release (ER) Formulation In Pediatric Subjects With Acute Otitis Media (AOM)****Summary**

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2014-004164-38   |
| Trial protocol           | Outside EU/EEA   |
| Global end of trial date | 18 February 2009 |

**Results information**

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 30 May 2016  |
| First version publication date | 15 July 2015 |

**Trial information****Trial identification**

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | A0661190 |
|-----------------------|----------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00796224 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Pfizer Inc.  |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017   |
| Public contact               | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc, 001 800-718-1021, ClinicalTrials.govCallCenter@pfizer.com |
| Scientific contact           | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc, 001 800-718-1021, ClinicalTrials.govCallCenter@pfizer.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? | Yes |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 23 July 2009     |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 18 February 2009 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To compare the pharmacokinetics of azithromycin following a single dose of either 30 milligram per kilogram (mg/kg) IR or 60 mg/kg ER formulation in pediatric subjects with AOM.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 23 December 2008 |
| 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 | Costa Rica: 38 |
| Worldwide total number of subjects   | 38             |
| EEA total number of subjects         | 0              |

Notes:

### Subjects enrolled per age group

|   |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 19 |
| Children (2-11 years)                     | 19 |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Study started on 23 December 2008 and completed on 18 February 2009 in Costa Rica. Subjects were screened within 48 hours of dosing.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | 60 mg/kg Azithromycin Extended-release (ER) |

Arm description:

Subjects received Azithromycin ER single oral dose on Day 1.

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

Dosage and administration details:

Subjects received 60 mg/kg Azithromycin ER single oral dose on Day 1.

|                  |  |
|------------------|--|
| <b>Arm title</b> | 30 mg/kg Azithromycin Immediate-release (IR) |
|------------------|--|

Arm description:

Subjects received Azithromycin IR single oral dose on Day 1.

|  |                 |
|--|-----------------|
| Arm type                               | Reference       |
| Investigational medicinal product name | Azithromycin    |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Oral suspension |
| Routes of administration               | Oral use        |

Dosage and administration details:

Subjects received 30 mg/kg Azithromycin IR single oral dose on Day 1.

| <b>Number of subjects in period 1</b> | 60 mg/kg<br>Azithromycin<br>Extended-release<br>(ER) | 30 mg/kg<br>Azithromycin<br>Immediate-release<br>(IR) |
|---------------------------------------|--|---|
| Started                               | 19   | 19  |
| Completed                             | 18   | 18  |
| Not completed                         | 1  | 1   |
| Adverse event                         | 1  | -   |

|                    |   |   |
|--------------------|---|---|
| Protocol Violation | - | 1 |
|--------------------|---|---|

## Baseline characteristics

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | 60 mg/kg Azithromycin Extended-release (ER) |
|-----------------------|---|

Reporting group description:

Subjects received Azithromycin ER single oral dose on Day 1.

|                       |  |
|-----------------------|--|
| Reporting group title | 30 mg/kg Azithromycin Immediate-release (IR) |
|-----------------------|--|

Reporting group description:

Subjects received Azithromycin IR single oral dose on Day 1.

| Reporting group values                | 60 mg/kg<br>Azithromycin<br>Extended-release<br>(ER) | 30 mg/kg<br>Azithromycin<br>Immediate-release<br>(IR) | Total |
|---------------------------------------|--|---|-------|
| Number of subjects                    | 19   | 19  | 38    |
| Age categorical<br>Units: Subjects    |  |   |       |
| 1 month to less than (<) 2 years      | 13   | 6   | 19    |
| 2 years to <12 years                  | 6  | 13  | 19    |
| Gender categorical<br>Units: Subjects |  |   |       |
| Female                                | 8  | 7   | 15    |
| Male                                  | 11   | 12  | 23    |

## End points

### End points reporting groups

|                              |  |
|------------------------------|--|
| Reporting group title        | 60 mg/kg Azithromycin Extended-release (ER)                  |
| Reporting group description: | Subjects received Azithromycin ER single oral dose on Day 1. |
| Reporting group title        | 30 mg/kg Azithromycin Immediate-release (IR)                 |
| Reporting group description: | Subjects received Azithromycin IR single oral dose on Day 1. |

### Primary: Area Under the Curve From Time Zero to 72 Hours (AUC72Hours)

|                        |  |
|------------------------|--|
| End point title        | Area Under the Curve From Time Zero to 72 Hours (AUC72Hours)   |
| End point description: | AUC72 = Area under the plasma concentration versus time curve from time zero (pre-dose) to 72 hours. All subjects randomized and treated who had at least 1 of the pharmacokinetic parameters of primary interest. |
| End point type         | Primary  |
| End point timeframe:   | Pre-dose/ 0 to 72 hours  |

| End point values                               | 60 mg/kg Azithromycin Extended-release (ER) | 30 mg/kg Azithromycin Immediate-release (IR) |  |  |
|--|---|--|--|--|
| Subject group type                             | Reporting group                             | Reporting group                              |  |  |
| Number of subjects analysed                    | 18  | 18   |  |  |
| Units: nanogram*hour per milliliter (ng*hr/mL) |   |  |  |  |
| arithmetic mean (standard deviation)           | 12173.02 (± 6305.032)                       | 7950.949 (± 4759.301)                        |  |  |

### Statistical analyses

|                                   |   |
|-----------------------------------|---|
| Statistical analysis title        | Analysis of AUC72   |
| Statistical analysis description: | Test (60 mg/kg Azithromycin ER)/ Reference (30 mg/kg Azithromycin IR). Analysis of variance (ANOVA) method was used for analysis. |
| Comparison groups                 | 60 mg/kg Azithromycin Extended-release (ER) v 30 mg/kg Azithromycin Immediate-release (IR)  |

|   |                          |
|---|--------------------------|
| Number of subjects included in analysis | 36                       |
| Analysis specification                  | Pre-specified            |
| Analysis type                           | equivalence              |
| Parameter estimate                      | Ratio of Geometric Means |
| Point estimate                          | 157.98                   |
| Confidence interval                     |                          |
| level                                   | 90 %                     |
| sides                                   | 2-sided                  |
| lower limit                             | 98.87                    |
| upper limit                             | 252.44                   |

### Secondary: Area Under the Curve From Time Zero to Extrapolated Infinite Time (AUC Inf)

|                 |   |
|-----------------|---|
| End point title | Area Under the Curve From Time Zero to Extrapolated Infinite Time (AUC Inf) |
|-----------------|---|

End point description:

AUCinf = AUClast + (Clast\* divided by kel), where AUClast is calculated by Linear-Log trapezoidal method, Clast\* is the predicted serum concentration at the last quantifiable time point estimated from the log-linear regression analysis and kel is the terminal phase rate constant calculated by a linear regression of the log-linear concentration-time curve. All subjects randomized and treated who had at least 1 of the pharmacokinetic parameters of primary interest.

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

End point timeframe:

Pre-dose /0, 1, 2, 3, 4, 8, 24, 48, 72 hours post-dose

| End point values                     | 60 mg/kg<br>Azithromycin<br>Extended-<br>release (ER) | 30 mg/kg<br>Azithromycin<br>Immediate-<br>release (IR) |  |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed          | 18  | 18   |  |  |
| Units: ng*hr/mL                      |   |  |  |  |
| arithmetic mean (standard deviation) | 15536.19 (±<br>9310.399)                              | 9645.63 (±<br>6062.67)                                 |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum Observed Plasma Concentration (Cmax) of Azithromycin

|                 |  |
|-----------------|--|
| End point title | Maximum Observed Plasma Concentration (Cmax) of Azithromycin |
|-----------------|--|

End point description:

All subjects randomized and treated who had at least 1 of the pharmacokinetic parameters of primary interest.

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

End point timeframe:

Pre-dose/0, 1, 2, 3, 4, 8, 24, 48, 72 hours

| <b>End point values</b>              | 60 mg/kg<br>Azithromycin<br>Extended-<br>release (ER) | 30 mg/kg<br>Azithromycin<br>Immediate-<br>release (IR) |  |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed          | 18  | 18   |  |  |
| Units: ng/mL                         |   |  |  |  |
| arithmetic mean (standard deviation) | 774.75 (±<br>477.989)                                 | 901.644 (±<br>600.682)                                 |  |  |

### Statistical analyses

| <b>Statistical analysis title</b>  | Analysis of Cmax   |
|--|--|
| Statistical analysis description:<br>ANOVA method was used for analysis. |  |
| Comparison groups  | 30 mg/kg Azithromycin Immediate-release (IR) v 60 mg/kg Azithromycin Extended-release (ER) |
| Number of subjects included in analysis                                  | 36   |
| Analysis specification   | Pre-specified  |
| Analysis type  | equivalence  |
| Parameter estimate   | Ratio of Geometric Means   |
| Point estimate   | 91.63  |
| Confidence interval  |  |
| level  | 90 %   |
| sides  | 2-sided  |
| lower limit  | 56.21  |
| upper limit  | 149.38   |

### Secondary: Time to Reach Maximum Observed Plasma Concentration (Tmax) and Plasma Decay Half Life (t1/2) of Azithromycin

| <b>End point title</b>  | Time to Reach Maximum Observed Plasma Concentration (Tmax) and Plasma Decay Half Life (t1/2) of Azithromycin |
|---|--|
| End point description:<br>Plasma decay half-life is the time measured for the plasma concentration to decrease by one-half. All subjects randomized and treated who had at least 1 of the pharmacokinetic parameters of primary interest. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Pre dose/0, 1, 2, 3, 4, 8, 24, 48, 72 hours post-dose   |  |

| <b>End point values</b>       | 60 mg/kg<br>Azithromycin<br>Extended-<br>release (ER) | 30 mg/kg<br>Azithromycin<br>Immediate-<br>release (IR) |  |  |
|-------------------------------|---|--|--|--|
| Subject group type            | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed   | 18  | 18   |  |  |
| Units: hour                   |   |  |  |  |
| median (full range (min-max)) |   |  |  |  |
| Tmax                          | 3 (2 to 8)  | 2 (1 to 4.05)  |  |  |
| t1/2                          | 30.303 (15 to 52.2)                                   | 28.959 (10.4 to 49)                                    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Serum Concentrations of Azithromycin ER (Test) and Azithromycin IR (Reference)

|                        |   |
|------------------------|---|
| End point title        | Serum Concentrations of Azithromycin ER (Test) and Azithromycin IR (Reference)                                |
| End point description: | All subjects randomized and treated who had at least 1 of the pharmacokinetic parameters of primary interest. |
| End point type         | Secondary   |
| End point timeframe:   | 1, 2, 3, 4, 8, 24, 48, 72 hours   |

| <b>End point values</b>              | 60 mg/kg<br>Azithromycin<br>Extended-<br>release (ER) | 30 mg/kg<br>Azithromycin<br>Immediate-<br>release (IR) |  |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed          | 18  | 18   |  |  |
| Units: ng/mL                         |   |  |  |  |
| number (not applicable)              |   |  |  |  |
| Serum Concentration 1 hour post dose | 99.96   | 152.75   |  |  |
| Serum Concentration 2 hour postdose  | 293.14  | 579.72   |  |  |
| Serum concentration 3 hour postdose  | 381.96  | 381.69   |  |  |
| Serum Concentration 4 hour postdose  | 441.79  | 267.86   |  |  |
| Serum Concentration 8 hour postdose  | 244.75  | 140.33   |  |  |
| Serum Concentration 24 hour postdose | 142.41  | 82.31  |  |  |
| Serum Concentration 48 hour postdose | 94.79   | 50.06  |  |  |
| Serum Concentration 72 hour postdose | 56.03   | 30.6   |  |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Serum Concentration 1 hour postdose  |
| Statistical analysis description:<br>Ratio (percent) = Test/Reference multiplied by 100. ANOVA method was used for analysis. |  |
| Comparison groups  | 60 mg/kg Azithromycin Extended-release (ER) v 30 mg/kg Azithromycin Immediate-release (IR) |
| Number of subjects included in analysis  | 36   |
| Analysis specification   | Pre-specified  |
| Analysis type  | equivalence  |
| Parameter estimate   | Ratio of Geometric means (percent)   |
| Point estimate   | 65.44  |
| Confidence interval  |  |
| level  | 90 %   |
| sides  | 2-sided  |
| lower limit  | 23.56  |
| upper limit  | 181.77   |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Serum Concentration 2 hour postdose  |
| Statistical analysis description:<br>Ratio (percent) = Test/Reference multiplied by 100. ANOVA method was used for analysis. |  |
| Comparison groups  | 60 mg/kg Azithromycin Extended-release (ER) v 30 mg/kg Azithromycin Immediate-release (IR) |
| Number of subjects included in analysis  | 36   |
| Analysis specification   | Pre-specified  |
| Analysis type  | equivalence  |
| Parameter estimate   | Ratio of Geometric means (percent)   |
| Point estimate   | 50.57  |
| Confidence interval  |  |
| level  | 90 %   |
| sides  | 2-sided  |
| lower limit  | 25.24  |
| upper limit  | 101.3  |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Serum Concentration 3 hour postdose  |
| Statistical analysis description:<br>Ratio (percent) = Test/Reference multiplied by 100. ANOVA method was used for analysis. |  |
| Comparison groups  | 60 mg/kg Azithromycin Extended-release (ER) v 30 mg/kg Azithromycin Immediate-release (IR) |
| Number of subjects included in analysis  | 36   |
| Analysis specification   | Pre-specified  |
| Analysis type  | equivalence  |
| Parameter estimate   | Ratio of Geometric means (percent)   |
| Point estimate   | 100.07   |
| Confidence interval  |  |
| level  | 90 %   |
| sides  | 2-sided  |
| lower limit  | 57.91  |
| upper limit  | 172.92   |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Serum Concentration 4 hour postdose  |
| Statistical analysis description:<br>Ratio (percent) = Test/Reference multiplied by 100. ANOVA method was used for analysis. |  |
| Comparison groups  | 60 mg/kg Azithromycin Extended-release (ER) v 30 mg/kg Azithromycin Immediate-release (IR) |
| Number of subjects included in analysis  | 36   |
| Analysis specification   | Pre-specified  |
| Analysis type  | equivalence  |
| Parameter estimate   | Ratio of Geometric means (percent)   |
| Point estimate   | 164.93   |
| Confidence interval  |  |
| level  | 90 %   |
| sides  | 2-sided  |
| lower limit  | 103.78   |
| upper limit  | 262.12   |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Serum Concentration 8 hour postdose  |
| Statistical analysis description:<br>Ratio (percent) = Test/Reference multiplied by 100. ANOVA method was used for analysis. |  |
| Comparison groups  | 60 mg/kg Azithromycin Extended-release (ER) v 30 mg/kg Azithromycin Immediate-release (IR) |
| Number of subjects included in analysis  | 36   |
| Analysis specification   | Pre-specified  |
| Analysis type  | equivalence  |
| Parameter estimate   | Ratio of Geometric means (percent)   |
| Point estimate   | 174.41   |
| Confidence interval  |  |
| level  | 90 %   |
| sides  | 2-sided  |
| lower limit  | 110.07   |
| upper limit  | 276.36   |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Serum Concentration 24 hour postdose   |
| Statistical analysis description:<br>Ratio (percent) = Test/Reference multiplied by 100. ANOVA method was used for analysis. |  |
| Comparison groups  | 60 mg/kg Azithromycin Extended-release (ER) v 30 mg/kg Azithromycin Immediate-release (IR) |
| Number of subjects included in analysis  | 36   |
| Analysis specification   | Pre-specified  |
| Analysis type  | equivalence  |
| Parameter estimate   | Ratio of Geometric means (percent)   |
| Point estimate   | 173.01   |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 90 %    |
| sides               | 2-sided |
| lower limit         | 111.45  |
| upper limit         | 268.55  |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Serum Concentration 48 hour postdose   |
| Statistical analysis description:<br>Ratio (percent) = Test/Reference multiplied by 100. ANOVA method was used for analysis. |  |
| Comparison groups  | 60 mg/kg Azithromycin Extended-release (ER) v 30 mg/kg Azithromycin Immediate-release (IR) |
| Number of subjects included in analysis  | 36   |
| Analysis specification   | Pre-specified  |
| Analysis type  | equivalence  |
| Parameter estimate   | Ratio of Geometric means (percent)   |
| Point estimate   | 189.35   |
| Confidence interval  |  |
| level  | 90 %   |
| sides  | 2-sided  |
| lower limit  | 129.76   |
| upper limit  | 276.3  |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Serum Concentration 72 hour postdose   |
| Statistical analysis description:<br>Ratio (percent) = Test/Reference multiplied by 100. ANOVA method was used for analysis. |  |
| Comparison groups  | 60 mg/kg Azithromycin Extended-release (ER) v 30 mg/kg Azithromycin Immediate-release (IR) |
| Number of subjects included in analysis  | 36   |
| Analysis specification   | Pre-specified  |
| Analysis type  | equivalence  |
| Parameter estimate   | Ratio of Geometric means (percent)   |
| Point estimate   | 183.14   |
| Confidence interval  |  |
| level  | 90 %   |
| sides  | 2-sided  |
| lower limit  | 124.61   |
| upper limit  | 269.14   |

## Secondary: Number of Subjects With a Clinical Response

|  |   |
|--|---|
| End point title  | Number of Subjects With a Clinical Response |
| End point description:<br>Clinical response was assessed between Days 7 and 10, or when subjects discontinued the study prematurely (if applicable). Response was assessed by the investigator as cure or failure. Cure = Clinical signs and symptoms related to the acute illness have resolved, or clinical improvement is such that no additional therapy is necessary. Failure = One or more of the following: Signs and symptoms related to |   |

the acute illness have persisted or worsened and additional therapy is necessary; New clinical signs and symptoms of acute illness have developed and additional therapy is necessary. Any worsening of existing signs and symptoms, or new signs and symptoms, were documented as adverse events.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Day 7, 8, 9 or 10    |           |

| End point values            | 60 mg/kg<br>Azithromycin<br>Extended-<br>release (ER) | 30 mg/kg<br>Azithromycin<br>Immediate-<br>release (IR) |  |  |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed | 18  | 18   |  |  |
| Units: subjects             |   |  |  |  |
| Cure                        | 18  | 16   |  |  |
| Failure                     | 0   | 2  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Adverse Events (AEs) and Serious AEs (SAEs)

|   |   |
|---|---|
| End point title   | Adverse Events (AEs) and Serious AEs (SAEs) |
| End point description:  |   |
| All observed or volunteered AEs and SAEs regardless of treatment group or suspected causal relationship to the investigational product(s) was reported. All subjects who received at least 1 dose of study medication were included in the safety analyses. |   |
| End point type  | Secondary                                   |
| End point timeframe:  |   |
| Baseline up to 35 days of last study treatment  |   |

| End point values            | 60 mg/kg<br>Azithromycin<br>Extended-<br>release (ER) | 30 mg/kg<br>Azithromycin<br>Immediate-<br>release (IR) |  |  |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group                                       | Reporting group  |  |  |
| Number of subjects analysed | 19  | 19   |  |  |
| Units: subjects             |   |  |  |  |
| AEs                         | 4   | 5  |  |  |
| SAEs                        | 0   | 0  |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From baseline till 35 days after last study treatment

Adverse event reporting additional description:

EU BR specific AE tables were generated separately as per EU format. Latest coding dictionary has been used for EU BR tables.

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

### Dictionary used

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

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

### Reporting groups

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | 60 mg/kg Azithromycin ER |
|-----------------------|--------------------------|

Reporting group description:

Subjects received 60 mg/kg Azithromycin ER single oral dose on Day 1.

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | 30 mg/kg Azithromycin IR |
|-----------------------|--------------------------|

Reporting group description:

Subjects received 30 mg/kg Azithromycin IR single oral dose on Day 1.

| <b>Serious adverse events</b>                     | 60 mg/kg<br>Azithromycin ER | 30 mg/kg<br>Azithromycin IR |  |
|---|-----------------------------|-----------------------------|--|
| Total subjects affected by serious adverse events |                             |                             |  |
| subjects affected / exposed                       | 0 / 19 (0.00%)              | 0 / 19 (0.00%)              |  |
| number of deaths (all causes)                     | 0                           | 0                           |  |
| number of deaths resulting from adverse events    | 0                           | 0                           |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                     | 60 mg/kg<br>Azithromycin ER | 30 mg/kg<br>Azithromycin IR |  |
|---|-----------------------------|-----------------------------|--|
| Total subjects affected by non-serious adverse events |                             |                             |  |
| subjects affected / exposed                           | 4 / 19 (21.05%)             | 5 / 19 (26.32%)             |  |
| General disorders and administration site conditions  |                             |                             |  |
| Treatment failure                                     |                             |                             |  |
| subjects affected / exposed                           | 0 / 19 (0.00%)              | 2 / 19 (10.53%)             |  |
| occurrences (all)                                     | 0                           | 2                           |  |
| Gastrointestinal disorders                            |                             |                             |  |
| Diarrhoea   |                             |                             |  |

|  |                      |                     |  |
|--|----------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 19 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1 |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)   | 1 / 19 (5.26%)<br>1  | 0 / 19 (0.00%)<br>0 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 3 / 19 (15.79%)<br>3 | 1 / 19 (5.26%)<br>1 |  |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 0 / 19 (0.00%)<br>0  | 1 / 19 (5.26%)<br>1 |  |

## **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