



## Clinical trial results:

**A randomized, double-blind, multicenter, superiority Phase III study to assess the safety and efficacy of Topical Retapamulin Ointment 1%, applied twice daily versus Placebo Ointment in Adults and Children in the treatment of Secondarily- Infected Traumatic Lesions**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2015-004903-22  |
| Trial protocol           | Outside EU/EEA  |
| Global end of trial date | 02 October 2009 |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 29 December 2016 |
| First version publication date | 29 December 2016 |

### Trial information

#### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | TOC110977 |
|-----------------------|-----------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | GlaxoSmithKline  |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, |
| Public contact               | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,      |
| Scientific contact           | GSK Response Center, GlaxoSmithKline, 1 866-435-7343,      |

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:

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**Results analysis stage**

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 23 December 2009 |
| Is this the analysis of the primary completion data? | No               |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 02 October 2009 |
| Was the trial ended prematurely? | No              |

Notes:

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**General information about the trial**

Main objective of the trial:

TBD

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 21 May 2008 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | No          |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Argentina: 21      |
| Country: Number of subjects enrolled | Brazil: 4          |
| Country: Number of subjects enrolled | India: 42          |
| Country: Number of subjects enrolled | South Africa: 236  |
| Country: Number of subjects enrolled | United States: 204 |
| Worldwide total number of subjects   | 507                |
| EEA total number of subjects         | 0                  |

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)  | 6   |
| Children (2-11 years)                     | 82  |
| Adolescents (12-17 years)                 | 34  |
| Adults (18-64 years)                      | 362 |
| From 65 to 84 years                       | 21  |

|                   |   |
|-------------------|---|
| 85 years and over | 2 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 508 participants were randomized. One participant did not receive treatment; thus, no data were collected for this participant. Only 507 participants were included in the analysis.

### Period 1

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

### Arms

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

Arm description:

Topical retapamulin ointment, 1% twice daily for 5 days

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Retapamulin  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Ointment     |
| Routes of administration               | Topical use  |

Dosage and administration details:

This was provided as approximately 10 grams of an off-white smooth ointment and was applied to the infected lesion(s) at a dose of approximately 10 mg per cm<sup>2</sup> twice daily for 5 days; the maximum amount applied per application was to be approximately 1 gram

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

Arm description:

Matching placebo

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

Dosage and administration details:

This was provided as approximately 10 grams of an off-white smooth ointment and was applied to the infected lesion(s) at a dose of approximately 10 mg per cm<sup>2</sup> twice daily for 5 days; the maximum amount applied per application was to be approximately 1 gram

| <b>Number of subjects in period 1</b> | Retapamulin | Placebo |
|---------------------------------------|-------------|---------|
| Started                               | 343         | 164     |
| Completed                             | 322         | 141     |
| Not completed                         | 21          | 23      |
| Physician decision                    | 2           | -       |
| Consent withdrawn by subject          | 1           | 2       |
| Adverse event, non-fatal              | 4           | 3       |
| Unknown                               | 1           | 2       |
| Lost to follow-up                     | 2           | 1       |
| Lack of efficacy                      | 10          | 15      |
| Protocol deviation                    | 1           | -       |

## Baseline characteristics

### Reporting groups

|   |             |
|---|-------------|
| Reporting group title                                   | Retapamulin |
| Reporting group description:                            |             |
| Topical retapamulin ointment, 1% twice daily for 5 days |             |
| Reporting group title                                   | Placebo     |
| Reporting group description:                            |             |
| Matching placebo  |             |

| Reporting group values | Retapamulin | Placebo | Total |
|------------------------|-------------|---------|-------|
| Number of subjects     | 343         | 164     | 507   |
| Age categorical        |             |         |       |
| Units: Subjects        |             |         |       |

|   |         |         |     |
|---|---------|---------|-----|
| Age continuous                            |         |         |     |
| Age continuous description                |         |         |     |
| Units: years                              |         |         |     |
| arithmetic mean                           | 32.6    | 28.6    |     |
| standard deviation                        | ± 18.77 | ± 18.32 | -   |
| Gender categorical                        |         |         |     |
| Gender categorical description            |         |         |     |
| Units: Subjects                           |         |         |     |
| Female                                    | 144     | 63      | 207 |
| Male                                      | 199     | 101     | 300 |
| Race/Ethnicity, Customized                |         |         |     |
| Units: Subjects                           |         |         |     |
| African American/African Heritage         | 144     | 71      | 215 |
| American Indian or Alaskan Native         | 9       | 3       | 12  |
| Asian - Central / South Asian Heritage    | 0       | 1       | 1   |
| Asian - East Asian Heritage               | 4       | 2       | 6   |
| Asian - South East Asian Heritage         | 33      | 15      | 48  |
| Native Hawaiian or Other Pacific Islander | 1       | 2       | 3   |
| White - Arabic/North African Heritage     | 1       | 0       | 1   |
| White - White/Caucasian/European Heritage | 132     | 61      | 193 |
| Mixed Race                                | 19      | 9       | 28  |

## End points

### End points reporting groups

|   |             |
|---|-------------|
| Reporting group title                                   | Retapamulin |
| Reporting group description:                            |             |
| Topical retapamulin ointment, 1% twice daily for 5 days |             |
| Reporting group title                                   | Placebo     |
| Reporting group description:                            |             |
| Matching placebo  |             |

### Primary: Number of Participants with Clinical Success and Failure at Follow-up (7-9 days post therapy) for the Primary Efficacy Population

|  |   |
|--|---|
| End point title  | Number of Participants with Clinical Success and Failure at Follow-up (7-9 days post therapy) for the Primary Efficacy Population |
| End point description:<br>"Clinical Success" at follow-up was defined as "Resolution of clinically meaningful signs and symptoms of infection recorded at baseline including a pus/exudate Skin Infection Rating Scale (SIRS) score of "0". Clinical response at follow-up was classified as "Clinical Failure" for all other cases. The SIRS consists of seven items (pus/exudates, crusting, erythema/inflammation, tissue warmth, tissue edema, itching and pain). Each item has a score ranging from 0 to 6 (0=absent, 6=severe). The SIRS total score was calculated as the sum of the scores of all 7 SIRS items. Primary Efficacy Population: ITTC participants with base line pus/exudate $\geq 3$ who were enrolled under the original protocol with data captured under eCRF V1 and who were enrolled under protocol amendments with data captured under eCRF V2; ITTC (Intent-to-treat Clinical): all randomized par. who received at least one dose of study medication. |   |
| End point type   | Primary   |
| End point timeframe:<br>Days 12-14   |   |

| End point values            | Retapamulin        | Placebo         |  |  |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type          | Reporting group    | Reporting group |  |  |
| Number of subjects analysed | 246 <sup>[1]</sup> | 113             |  |  |
| Units: participants         |                    |                 |  |  |
| Clinical Success            | 184                | 75              |  |  |
| Clinical Failure            | 62                 | 38              |  |  |

Notes:

[1] - Primary Efficacy Population

### Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups          | Retapamulin v Placebo  |

|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 359                  |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| P-value                                 | = 0.098              |
| Method                                  | Chi-squared          |
| Parameter estimate                      | Risk difference (RD) |
| Point estimate                          | 8.4                  |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | -1.6                 |
| upper limit                             | 18.4                 |

### Secondary: Number of Participants with Clinical Success and Failure at Follow-up (7-9 days post therapy) for the Intent-to-Treat Bacteriology (ITTb) subset of the Primary Efficacy Population

|                 |   |
|-----------------|---|
| End point title | Number of Participants with Clinical Success and Failure at Follow-up (7-9 days post therapy) for the Intent-to-Treat Bacteriology (ITTb) subset of the Primary Efficacy Population |
|-----------------|---|

End point description:

"Clinical Success" at follow-up was defined as "Resolution of clinically meaningful signs and symptoms of infection recorded at baseline including a pus/exudate Skin Infection Rating Scale (SIRS) score of "0". Clinical response at follow-up was classified as "Clinical Failure" for all other cases. The SIRS consists of seven items (pus/exudates, crusting, erythema/inflammation, tissue warmth, tissue edema, itching and pain). Each item has a score ranging from 0 to 6 (0=absent, 6=severe). The SIRS total score was calculated as the sum of the scores of all 7 SIRS items. ITTB subset of Primary Efficacy Population: participants in the Primary Efficacy Population (see analysis population description in the Primary Outcome section) who had at least one pathogen isolated at the base line visit.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Days 12-14           |           |

| End point values            | Retapamulin        | Placebo         |  |  |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type          | Reporting group    | Reporting group |  |  |
| Number of subjects analysed | 182 <sup>[2]</sup> | 84              |  |  |
| Units: participants         |                    |                 |  |  |
| Clinical Success            | 139                | 54              |  |  |
| Clinical Failure            | 43                 | 30              |  |  |

Notes:

[2] - ITTB subset of Primary Efficacy Population

### Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups          | Placebo v Retapamulin  |



|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 266                  |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| P-value                                 | = 0.04               |
| Method                                  | Chi-squared          |
| Parameter estimate                      | Risk difference (RD) |
| Point estimate                          | 12.1                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 0.6                  |
| upper limit                             | 23.6                 |

### Secondary: Number of Participants with Microbiological Success and Failure at Follow-up (7-9 days post therapy)

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Microbiological Success and Failure at Follow-up (7-9 days post therapy) |
|-----------------|--|

End point description:

The "by pathogen" microbiological outcome was determined by comparing the baseline culture results to those at follow-up. The "by subject" microbiological response was "Microbiological Success" if the microbiological outcomes for all baseline pathogens (bps) belong to "Eradication" (elimination of bps), "Presumed Eradication" (clinical outcome was success; no culture was obtained due to lack of culturable material), or "Colonization" (previously unidentified pathogen is identified at end of therapy in participant who is resolved/improved); otherwise, response was "Microbiological Failure".

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

End point timeframe:

Days 12-14

| End point values            | Retapamulin        | Placebo         |  |  |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type          | Reporting group    | Reporting group |  |  |
| Number of subjects analysed | 182 <sup>[3]</sup> | 84              |  |  |
| Units: participants         |                    |                 |  |  |
| Microbiological Success     | 139                | 54              |  |  |
| Microbiological Failure     | 43                 | 30              |  |  |

Notes:

[3] - ITTB subset of Primary Efficacy Population

### Statistical analyses

|                            |                        |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Comparison groups          | Placebo v Retapamulin  |

|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 266                  |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| P-value                                 | = 0.04               |
| Method                                  | Chi-squared          |
| Parameter estimate                      | Risk difference (RD) |
| Point estimate                          | 12.1                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 0.6                  |
| upper limit                             | 23.6                 |

### Secondary: Number of Participants with the Indicated Clinical Outcome at End of Therapy (2-4 days post therapy)

|                 |  |
|-----------------|--|
| End point title | Number of Participants with the Indicated Clinical Outcome at End of Therapy (2-4 days post therapy) |
|-----------------|--|

End point description:

Clinical outcome is determined by the investigator based on signs and symptoms (S/S) at the end of therapy evaluation. The 4 clinical outcome categories are: clinical success, resolution of clinically meaningful S/S of infection recorded at baseline (BL), including a pus/exudates score of 0; clinical improvement, improvement of S/S of infection recorded at BL to such an extent that no further antimicrobial therapy is necessary; clinical failure, insufficient improvement or deterioration of S/S of infection recorded at BL such that additional antibiotic therapy is required; unable to determine.

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

End point timeframe:

Days 7-9

| End point values            | Retapamulin        | Placebo         |  |  |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type          | Reporting group    | Reporting group |  |  |
| Number of subjects analysed | 246 <sup>[4]</sup> | 113             |  |  |
| Units: participants         |                    |                 |  |  |
| Clinical Success            | 130                | 52              |  |  |
| Clinical Improvement        | 102                | 45              |  |  |
| Clinical Failure            | 11                 | 14              |  |  |
| Unable to Determine         | 3                  | 2               |  |  |

Notes:

[4] - Primary Efficacy Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Baseline Pathogens with the Indicated Microbiological Outcome at End of Therapy (2-4 days post therapy)

|                 |   |
|-----------------|---|
| End point title | Number of Baseline Pathogens with the Indicated Microbiological Outcome at End of Therapy (2-4 days post therapy) |
|-----------------|---|

End point description:

The "by pathogen" microbiological outcome was determined by comparing the baseline culture results to those at follow-up. The results presented below pooled all baseline pathogens (bps). Eradication: elimination of bps. Presumed Eradication: clinical outcome was success; no culture was obtained due to lack of culturable material. Presumed Improvement: clinical outcome was improvement such that no culture was obtained due to lack of culturable material. Persistence: bps still present. Presumed persistence: clinical failure and no culture was obtained.

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

End point timeframe:

Days 7-9

| End point values            | Retapamulin        | Placebo         |  |  |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type          | Reporting group    | Reporting group |  |  |
| Number of subjects analysed | 243 <sup>[5]</sup> | 110             |  |  |
| Units: baseline pathogens   |                    |                 |  |  |
| Eradication                 | 4                  | 5               |  |  |
| Presumed Eradication        | 137                | 49              |  |  |
| Presumed Improvement        | 94                 | 35              |  |  |
| Persistence                 | 3                  | 13              |  |  |
| Presumed Persistence        | 5                  | 8               |  |  |

Notes:

[5] - ITTB subset of Primary Efficacy Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Therapeutic Success and Failure at Follow-up (7-9 days post therapy)

|                 |  |
|-----------------|--|
| End point title | Number of Participants with Therapeutic Success and Failure at Follow-up (7-9 days post therapy) |
|-----------------|--|

End point description:

"Therapeutic Success (Succ)" was referred to as both "Clinical Succ" and "Microbiological (Micro) Succ" at Follow-up. "Clinical Succ" was the "Resolution of baseline signs/symptoms of infection with a pus score of "0." A participant was "Micro Succ" if the micro outcome for all baseline pathogens (bps) belonged to "Eradication" (elimination of bps), "Presumed Eradication" (clinical outcome is success; no culturable material), or "Colonization" (new pathogen is identified at end of therapy in participants who are resolved/improved). All other combinations were deemed "Therapeutic Failures."

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

End point timeframe:

Follow-up (Days 12-14)

| End point values            | Retapamulin        | Placebo         |  |  |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type          | Reporting group    | Reporting group |  |  |
| Number of subjects analysed | 182 <sup>[6]</sup> | 84              |  |  |
| Units: participants         |                    |                 |  |  |
| Success                     | 139                | 54              |  |  |
| Failure                     | 43                 | 30              |  |  |

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Notes:

[6] - ITTB subset of Primary Efficacy Population

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### **Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were recorded from the first dose of study medication until study completion. Serious AEs (SAEs) were collected from the time of consent and continued until study completion (including the Follow-up Period).

Adverse event reporting additional description:

AEs were collected for all randomized participants (par.) who received at least one dose of study medications (i.e., ITTC Population). Safety data were analyzed based on the actual treatment received. One par. who was randomized to retapamulin treatment but actually received placebo was included in the placebo arm for the safety analyses.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 12.1 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Retapamulin |
|-----------------------|-------------|

Reporting group description:

Topical retapamulin ointment, 1% twice daily for 5 days

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Matching placebo

| Serious adverse events                            | Retapamulin     | Placebo         |  |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events |                 |                 |  |
| subjects affected / exposed                       | 1 / 342 (0.29%) | 1 / 165 (0.61%) |  |
| number of deaths (all causes)                     | 0               | 0               |  |
| number of deaths resulting from adverse events    | 0               | 0               |  |
| Cardiac disorders                                 |                 |                 |  |
| Myocardial infarction                             |                 |                 |  |
| subjects affected / exposed                       | 1 / 342 (0.29%) | 0 / 165 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           |  |
| Infections and infestations                       |                 |                 |  |
| Pneumococcal pneumonia                            |                 |                 |  |
| subjects affected / exposed                       | 0 / 342 (0.00%) | 1 / 165 (0.61%) |  |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           |  |

| <b>Non-serious adverse events</b>                     | Retapamulin     | Placebo         |  |
|---|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                 |                 |  |
| subjects affected / exposed                           | 8 / 342 (2.34%) | 4 / 165 (2.42%) |  |
| Injury, poisoning and procedural complications        |                 |                 |  |
| Wound secretion                                       |                 |                 |  |
| subjects affected / exposed                           | 1 / 342 (0.29%) | 0 / 165 (0.00%) |  |
| occurrences (all)                                     | 1               | 0               |  |
| Nervous system disorders                              |                 |                 |  |
| Tension headache                                      |                 |                 |  |
| subjects affected / exposed                           | 0 / 342 (0.00%) | 1 / 165 (0.61%) |  |
| occurrences (all)                                     | 0               | 1               |  |
| General disorders and administration site conditions  |                 |                 |  |
| Application site pain                                 |                 |                 |  |
| subjects affected / exposed                           | 5 / 342 (1.46%) | 0 / 165 (0.00%) |  |
| occurrences (all)                                     | 5               | 0               |  |
| Condition aggravated                                  |                 |                 |  |
| subjects affected / exposed                           | 3 / 342 (0.88%) | 1 / 165 (0.61%) |  |
| occurrences (all)                                     | 3               | 1               |  |
| Pyrexia   |                 |                 |  |
| subjects affected / exposed                           | 0 / 342 (0.00%) | 3 / 165 (1.82%) |  |
| occurrences (all)                                     | 0               | 3               |  |
| Application site paraesthesia                         |                 |                 |  |
| subjects affected / exposed                           | 1 / 342 (0.29%) | 0 / 165 (0.00%) |  |
| occurrences (all)                                     | 1               | 0               |  |
| Application site pruritus                             |                 |                 |  |
| subjects affected / exposed                           | 1 / 342 (0.29%) | 0 / 165 (0.00%) |  |
| occurrences (all)                                     | 1               | 0               |  |
| Eye disorders   |                 |                 |  |
| Eye pruritus  |                 |                 |  |
| subjects affected / exposed                           | 1 / 342 (0.29%) | 0 / 165 (0.00%) |  |
| occurrences (all)                                     | 1               | 0               |  |
| Ocular hyperaemia                                     |                 |                 |  |
| subjects affected / exposed                           | 1 / 342 (0.29%) | 0 / 165 (0.00%) |  |
| occurrences (all)                                     | 1               | 0               |  |
| Gastrointestinal disorders                            |                 |                 |  |

|  |  |  |  |
|--|--|--|--|
| Nausea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 342 (0.00%)<br>0   | 1 / 165 (0.61%)<br>1   |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)   | 1 / 342 (0.29%)<br>1   | 0 / 165 (0.00%)<br>0   |  |
| Skin and subcutaneous tissue disorders<br>Dermatitis<br>subjects affected / exposed<br>occurrences (all)   | 1 / 342 (0.29%)<br>1   | 0 / 165 (0.00%)<br>0   |  |
| Renal and urinary disorders<br>Haematuria<br>subjects affected / exposed<br>occurrences (all)  | 1 / 342 (0.29%)<br>1   | 0 / 165 (0.00%)<br>0   |  |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 342 (0.29%)<br>1   | 0 / 165 (0.00%)<br>0   |  |
| Infections and infestations<br>Abscess<br>subjects affected / exposed<br>occurrences (all)<br><br>Cellulitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 342 (0.29%)<br>1<br><br>0 / 342 (0.00%)<br>0<br><br>1 / 342 (0.29%)<br>1<br><br>0 / 342 (0.00%)<br>0 | 0 / 165 (0.00%)<br>0<br><br>1 / 165 (0.61%)<br>1<br><br>0 / 165 (0.00%)<br>0<br><br>1 / 165 (0.61%)<br>1 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 25 November 2008 | This amendment was conducted to: make a change to the entry criterion regarding minimum pus/exudate SIRS score; revise the exclusion criterion regarding surgical intervention and other investigational drug use; amend information provided in the introduction; and, re-define and re-classify clinical and microbiological outcomes at the end of therapy and follow-up visits. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported