# EU Clinical Trials Register

## Clinical trial results:
## Randomised, prospective, double-dummy double-blinded study to evaluate safety and efficacy of Angocin Anti-Infekt N versus standard antibiotics in the treatment of acute uncomplicated cystitis

### Summary

| | |
|---|---|
| EudraCT number | 2010-022096-54 |
| Trial protocol | DE |
| Global end of trial date | 14 June 2013 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 06 July 2022 |
| First version publication date | 06 July 2022 |

### Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | Repha_1344 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Repha GmbH |
| Sponsor organisation address | Alt-Godshorn 87, Langenhagen, Germany, 30855 |
| Public contact | CRO, Mediconomics GmbH, 049 05115609980, info@mediconomics.com |
| Scientific contact | CRO, Mediconomics GmbH, 049 05115609980, info@mediconomics.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 | 14 June 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 June 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 June 2013 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

Demonstration of the non-inferiority of ANGOCIN® Anti-Infekt N in comparison with two chemically defined standard antibiotics (cotrimoxazole and nitrofurantoin) in the therapy
of acute, uncomplicated cystitis.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice (GCP), which has its origins in the Declaration of Helsinki, and in strict compliance with the German
German Drug Law (AMG) and the German Federal Data Protection Act (BDSG),
in order to protect the rights, safety and well-being of patients.

Background therapy: -

Evidence for comparator:

The choice of the standard antibiotic was Kepinol® forte, as it is currently the most frequently prescribed antibiotic in
Germany for UTIs and is recommended by the DGGG (Deutsche Gesellschaft für Gynäkologie und Geburtshilfe), among others. The comparison with cotrimoxazole and nitrofurantoin was planned in two stages:
1st stage : Kepinol® forte.
2nd stage : preparation with the active substance nitrofurantoin.
The 1st stage was terminated without the planned number of patients being reached,
the 2nd stage was not started.

| | |
|---|---|
| Actual start date of recruitment | 18 May 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Scientific research |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Germany: 96 |
| Worldwide total number of subjects | 96 |
| EEA total number of subjects | 96 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |

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

# Subject disposition

## Recruitment

Recruitment details:

This study was conducted in two parts: controlled phase and optional follow-up

## Pre-assignment

Screening details:

When a patient was enrolled in the study, he or she was assigned a consecutive screening number within the centres. Via the patient number = "centre number
/ screening number", each patient in the study is clearly identifiable. In total, 96 patients were screened and 96 patients were randomized.

## Period 1

| | |
|---|---|
| Period 1 title | Controlled phase |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

As control and comparator differed with regard to the galenic properties, the trial was conducted in a doubly-dummy design. Despite differing treatment durations, the overall study medication intake was the same in both treatment arms as ensured by the double dummy design.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Investigational product |

Arm description:

Group 1
morning:     5x Investigational product plus 1x placebo
noon:          5x investigational product
afternoon: 5x invstigatioal product
evening:     5x investigational product plus 1x placebo

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Angocin Anti-Infekt N |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

morning:         5x Investigational product plus 1x placebo
noon:              5x investigational product
afternoon:      5x invstigatioal product
evening:          5x investigational product plus 1x placebo

| | |
|---|---|
| **Arm title** | Active Comparator |

Arm description:

morning:      5x placebo + 1x active comparator
noon:           5 x placebo
afternoon:   5 x placebo
evening:       5 x placebo + 1x active comparator

| | |
|---|---|
| Arm type | Active comparator |

| Investigational medicinal product name | Kepinol forte |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

morning:     5x placebo + 1x active comparator
noon:          5 x placebo
afternoon:  5 x placebo
evening:      5 x placebo + 1x active comparator

| **Number of subjects in period 1** | Investigational product | Active Comparator |
|---|---|---|
| Started | 45 | 51 |
| Completed | 22 | 29 |
| Not completed | 23 | 22 |
|    retrospective screening failure | 18 | 20 |
|    missing screening results | - | 1 |
|    Adverse event, non-fatal | 1 | - |
|    need for antibiotics | 2 | - |
|    personal reasons | - | 1 |
|    Lack of efficacy | 2 | - |

## Period 2

| Period 2 title | Optional follow-up phase |
|---|---|
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

Randomization was conducted in period 1

## Arms

| Are arms mutually exclusive? | Yes |
|---|---|
| **Arm title** | Investigational product |

Arm description: -

| Arm type | Experimental |
|---|---|
| Investigational medicinal product name | Angocin Anti-Infekt N |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

no intervention during follow-up

| Arm title | Active Comparator |
|---|---|
| Arm description: - | |
| Arm type | Active comparator |
| Investigational medicinal product name | Kepinol forte |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

no intervention during follow-up

| Number of subjects in period 2[1] | Investigational product | Active Comparator |
|---|---|---|
| Started | 19 | 25 |
| Completed | 17 | 24 |
| Not completed | 2 | 1 |
|     follow-up is optional | 2 | 1 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: The follow-up period was optional. The study was finished preliminary.

**Baseline characteristics**

## End points

### End points reporting groups

| Reporting group title | Investigational product |
|---|---|

Reporting group description:

Group 1
morning:    5x Investigational product plus 1x placebo
noon:       5x investigational product
afternoon: 5x invstigatioal product
evening:    5x investigational product plus 1x placebo

| Reporting group title | Active Comparator |
|---|---|

Reporting group description:

morning:    5x placebo + 1x active comparator
noon:       5 x placebo
afternoon:  5 x placebo
evening:    5 x placebo + 1x active comparator

| Reporting group title | Investigational product |
|---|---|

Reporting group description: -

| Reporting group title | Active Comparator |
|---|---|

Reporting group description: -

| Subject analysis set title | Per protocol |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

All subjects from the intention-to-treat population without elevant protocol breaches

| Subject analysis set title | ITT |
|---|---|
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

all subjects receiving study drug at least once. Same as the number of randomized subjects as well as safety population.

### Primary: Reduction in the number of lead cystitis germs from visit 1 (start of treatment) to visit 3 (follow-up 1), measured by the proportion of responders (definition: from > 10^5 cfu/mL midstream urine at visit 1 decrease to < 10^3 cfu/mL midstream urine

| End point title | Reduction in the number of lead cystitis germs from visit 1 (start of treatment) to visit 3 (follow-up 1), measured by the proportion of responders (definition: from > 10^5 cfu/mL midstream urine at visit 1 decrease to < 10^3 cfu/mL midstream urine |
|---|---|

End point description:

Reduction in the number of lead cystitis germs from visit 1 (start of treatment) to visit 3 (follow-up 1), measured by the proportion of responders (definition: from > 10^5 cfu/mL midstream urine at visit 1 decrease to < 10^3 cfu/mL midstream urine at visit 3).

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

End point timeframe:

from visit 1 (start of treatment) to visit 3 (follow-up 1)

| End point values | Investigational product | Active Comparator | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 29 | | |
| Units: number of responders | 10 | 15 | | |

## Statistical analyses

| Statistical analysis title | Primary endpoint |
|---|---|
| Comparison groups | Investigational product v Active Comparator |
| Number of subjects included in analysis | 51 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[1] |
| Parameter estimate | Mean difference (net) |
| Point estimate | -6.72 |
| Confidence interval | |
|     level | 95 % |
|     sides | 1-sided |
|     lower limit | -33.9 |

Notes:

[1] - The study was preliminary finished. However, based on the primary endpoint data available, a statistic analysis was performed. With a lower limit of the 95% CI of -33.90%  of the treatment difference -6.27%, the non-inferiority of Angocin vs. Kepinol could not be concluded because the lower CI does not fulfil the condition -10.00% < lower CI. Keeping in mind that only 51 patients (instead of 356 patients planned) completed the study these results are limited.

## Secondary: Change in general complaints and symptoms from visit 1 to visit 3

| End point title | Change in general complaints and symptoms from visit 1 to visit 3 |
|---|---|

End point description:

Change in number of general symptoms or complaints

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

End point timeframe:

visit 1 to visit 3

| End point values | Investigational product | Active Comparator | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 51 | | |
| Units: percentage of patients | 95 | 96 | | |

## Statistical analyses

| Statistical analysis title | General complaints and symptoms |
|---|---|

Statistical analysis description:

Decrease of signs of general complaints and symptoms

| Comparison groups | Investigational product v Active Comparator |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9275 |
| Method | Wilcoxon (Mann-Whitney) |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |

## Secondary: Duration until being symptom-free

| End point title | Duration until being symptom-free |
|---|---|

End point description:

Median of the time until subjects are symptom-free. ITT population. The duration until freedom from symptoms is defined as the time span (number of treatment days) until the disappearance of all complaints/symptoms that the patient should record in the diary from visit 1 to visit 2.

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

End point timeframe:

Visit 1 to Visit 2

| End point values | Investigational product | Active Comparator | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 44[2] | 51 | | |
| Units: median days | 7 | 4 | | |

Notes:

[2] - for one subject, diary was missing

## Statistical analyses

| Statistical analysis title | Time until being symptom-free |
|---|---|

Statistical analysis description:

Time until being symptom-free in the ITT set.

| Comparison groups | Investigational product v Active Comparator |
|---|---|
| Number of subjects included in analysis | 95 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.11 |
| Method | Chi-squared |
| Confidence interval | |
| level | 95 % |

## Secondary: Physicians' assessment of effectiveness at visit 3

| End point title | Physicians' assessment of effectiveness at visit 3 |
|---|---|

End point description:

Number of patients who have recovered at visit 3 in the PP set.

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

End point timeframe:

visit 3

| **End point values** | Investigational product | Active Comparator | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 29 | | |
| Units: Number of patients | 17 | 29 | | |

### Statistical analyses

| **Statistical analysis title** | Efficacy at visit 3 |
|---|---|
| Comparison groups | Investigational product v Active Comparator |
| Number of subjects included in analysis | 51 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.0313 |
| Method | Chi-squared |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |

### Secondary: Relapse frequency or new infections between visit 3 and visit 4

| End point title | Relapse frequency or new infections between visit 3 and visit 4 |
|---|---|

End point description:

number of patients who experience a relapse (reoccurence of signs and symptoms within 14 days)

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

End point timeframe:

visit 3 and visit 4

| **End point values** | Investigational product | Active Comparator | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 29 | | |
| Units: number of patients | 1 | 1 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Evaluation of the course of the disease by the physician on visit 2 (day 8)

| End point title | Evaluation of the course of the disease by the physician on visit 2 (day 8) |
|---|---|
| End point description: | |
| Number of patients without symptoms at visit 2, ITT-set | |
| End point type | Secondary |
| End point timeframe: | |
| visit 2 | |

| End point values | Investigational product | Active Comparator | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 51 | | |
| Units: number of patients recovered | 30 | 41 | | |

## Statistical analyses

| Statistical analysis title | Course of disease |
|---|---|
| Comparison groups | Active Comparator v Investigational product |
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.1067 |
| Method | Wilcoxon (Mann-Whitney) |

## Secondary: Change in dysuria from visit 1 to visit 3

| End point title | Change in dysuria from visit 1 to visit 3 |
|---|---|
| End point description: | |
| Decrease in signs of disease in dysuria | |
| End point type | Secondary |
| End point timeframe: | |
| visit 1 to visit 3 | |

| **End point values** | Investigational product | Active Comparator | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 51 | | |
| Units: percentage of patients | 95 | 94 | | |

**Statistical analyses**

| **Statistical analysis title** | Dysuria |
|---|---|
| Comparison groups | Investigational product v Active Comparator |
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.7585 |
| Method | Wilcoxon (Mann-Whitney) |

**Secondary: Change in pollakisuria from visit 1 to visit 3**

| End point title | Change in pollakisuria from visit 1 to visit 3 |
|---|---|
| End point description: | |
| Decrease in signs of pollakisuria | |
| End point type | Secondary |
| End point timeframe: | |
| visit 1 to visit 3 | |

| **End point values** | Investigational product | Active Comparator | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 51 | | |
| Units: percentage of patients | 98 | 94 | | |

**Statistical analyses**

| **Statistical analysis title** | Pollakisuria |
|---|---|
| Statistical analysis description: | |
| Decrease in pollakisuria score | |
| Comparison groups | Investigational product v Active Comparator |

| | |
|---|---|
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.3508 |
| Method | Wilcoxon (Mann-Whitney) |

## Secondary: Change in nocturia from visit 1 to visit 3

| | |
|---|---|
| End point title | Change in nocturia from visit 1 to visit 3 |
| End point description: | |
| Decrease in signs of nocturia | |
| End point type | Secondary |
| End point timeframe: | |
| visit 1 to visit 3 | |

| **End point values** | Investigational product | Active Comparator | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 51 | | |
| Units: percentage of patients | 93 | 93 | | |

### Statistical analyses

| **Statistical analysis title** | Nocturia |
|---|---|
| Statistical analysis description: | |
| Decrease in nocturia score | |
| Comparison groups | Investigational product v Active Comparator |
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.9302 |
| Method | Wilcoxon (Mann-Whitney) |

## Secondary: Change in urinary incontinence

| | |
|---|---|
| End point title | Change in urinary incontinence |
| End point description: | |
| Decrease in signs of disease in urinary incontinence | |
| End point type | Secondary |
| End point timeframe: | |
| visit 1 to visit 3 | |

| End point values | Investigational product | Active Comparator | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 51 | | |
| Units: percentage of subjects | 90 | 94 | | |

## Statistical analyses

| Statistical analysis title | Urinary incontinence |
|---|---|
| Statistical analysis description: | |
| Change in urinary incontinence score | |
| Comparison groups | Investigational product v Active Comparator |
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.6148 |
| Method | Wilcoxon (Mann-Whitney) |
| Parameter estimate | Mean difference (net) |

# Adverse events

## Adverse events information

| | |
|---|---|
| Timeframe for reporting adverse events: serious adverse events within 24 hours | |
| Assessment type | Systematic |

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 14.1 |

## Reporting groups

| | |
|---|---|
| Reporting group title | Investigational product |
| Reporting group description: Investigational drug | |
| Reporting group title | Active comparator |
| Reporting group description: Active comparator | |

| Serious adverse events | Investigational product | Active comparator | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 1 / 51 (1.96%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 51 (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 | | | |
| Appendicitis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 51 (1.96%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Investigational product | Active comparator | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | 6 / 51 (11.76%) | |
| Investigations | | | |
| C-reactive protein increased | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 51 (1.96%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Headache | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 1 / 51 (1.96%) | |
| occurrences (all) | 1 | 1 | |
| Disturbance in attention | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 51 (1.96%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 51 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain lower | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 51 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dyspepsia | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 51 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Constipation | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 51 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal pain | | | |

| | | | |
|---|---|---|---|
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 51 (1.96%) | |
| occurrences (all) | 0 | 1 | |
| Nausea | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 2 / 51 (3.92%) | |
| occurrences (all) | 0 | 2 | |
| Diarrhoea | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 51 (1.96%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 51 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Eczema | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 51 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin exfoliation | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 51 (1.96%) | |
| occurrences (all) | 0 | 1 | |
| Skin disorder | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 51 (1.96%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| Restlessness | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 51 (1.96%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |

| Flank pain | | | |
|---|---|---|---|
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 51 (1.96%) | |
| occurrences (all) | 0 | 1 | |

| Infections and infestations | | | |
|---|---|---|---|
| Pneumonia | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 51 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Upper respiratory tract infection | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 51 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| Metabolism and nutrition disorders | | | |
|---|---|---|---|
| Diabetes mellitus | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 51 (0.00%) | |
| occurrences (all) | 1 | 0 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol?  Yes

| Date | Amendment |
|---|---|
| 11 August 2011 | mainly addition of new study sites, addition of beta-defensin 2 investigation in one study center, prolongation of trial duration |
| 13 October 2011 | mainly addition of further study centers, prolongation of trial duration |
| 05 January 2012 | mainly addition of further study centers |
| 24 May 2012 | mainly inclusion of patients >65 years, omission of positive nitrite as inclusion criterium, prolongation of study duration |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial?  No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study was prematurely finalized due to deficient recruitment. Only one center (03)  fulfilled satisfying recruitment numbers. Responder rates in the remaining centres were below the rates of centre 03.

Notes:

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/28352615