



Clinical trial results:

A double-blind, double-dummy, prospective, randomized multiple-site study of oral Finafloxacin 300 mg b.i.d. versus oral Ciprofloxacin 250 mg b.i.d. in patients with lower uncomplicated UTI (uUTI) with a treatment duration of 3 days.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2007-007742-35 |
| Trial protocol | DE |
| Global end of trial date | 14 May 2009 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 23 December 2018 |
| First version publication date | 23 December 2018 |
| Summary attachment (see zip file) | CSR Synopsis FINA-003 (FINA-003_Syn_Final Version_1.0.pdf) |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | FINA-003 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00722735 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | MerLion Pharmaceuticals GmbH |
| Sponsor organisation address | Robert-Roessle-Str. 10, Berlin, Germany, 13125 |
| Public contact | Head Regulatory Affairs, MerLion Pharmaceuticals GmbH, lueckermann@merlionpharma.de |
| Scientific contact | Head Regulatory Affairs, MerLion Pharmaceuticals GmbH, lueckermann@merlionpharma.de |

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 | 08 February 2010 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 May 2009 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 May 2009 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To compare the bacteriological eradication rates of Finafloxacin and Ciprofloxacin in female patients with uUTI.

Protection of trial subjects:

Exclusion of subjects with abnormal ECG findings; continuous monitoring with 12-lead ECG.

Background therapy: -

Evidence for comparator:

Ciprofloxacin was chosen as a comparator since it is the most widely used fluoroquinolone in the treatment of urinary infections.

| | |
|---|-----------------|
| Actual start date of recruitment | 08 October 2008 |
| 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 | Germany: 24 |
| Country: Number of subjects enrolled | Singapore: 12 |
| Worldwide total number of subjects | 36 |
| EEA total number of subjects | 24 |

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) | 36 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

First patient enrolled on 08-OCT-2008 and last patient completed on 14-MAY-2009

Countries: Germany and Singapore

Pre-assignment

Screening details:

After signing the informed consent patient received screening no. If these patients are eligible to continue the study, based on the inclusion and exclusion criteria they will be assigned to one of the two treatment groups (Finafloxacin or Ciprofloxacin in a ratio 2:1).

Period 1

| | |
|------------------------------|---|
| Period 1 title | Overall Trial (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:

Blinding was conducted using the double-dummy technique.

Arms

| | |
|------------------------------|-------|
| Are arms mutually exclusive? | Yes |
| Arm title | Verum |

Arm description:

Finafloxacin 300 mg b.i.d. for 3 days

| | |
|--|----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Finafloxacin hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Finafloxacin 300 mg b.i.d (6 X 50 mg tablets) + Ciprofloxacin placebo (one capsule) b.i.d. for 3 days

| | |
|------------------|------------|
| Arm title | Comparator |
|------------------|------------|

Arm description:

Ciprofloxacin 250 mg b.i.d for 3 days

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Ciprofloxacin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

Ciprofloxacin, one capsule with 250 mg b.i.d. + Finafloxacin 6 placebo tablets b.i.d. for 3 days

| Number of subjects in period 1 | Verum | Comparator |
|---------------------------------------|-------|------------|
| Started | 28 | 8 |
| Completed | 25 | 8 |
| Not completed | 3 | 0 |
| Adverse event, non-fatal | 3 | - |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall Trial |
| Reporting group description: - | |

| Reporting group values | Overall Trial | Total | |
|--|---------------|-------|--|
| Number of subjects | 36 | 36 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 36 | 36 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 35.9 | | |
| standard deviation | ± 12.4 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 36 | 36 | |
| Male | 0 | 0 | |

Subject analysis sets

| | |
|--|-----------------------------|
| Subject analysis set title | Safety Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Patients that received at least one dose of study medication | |
| Subject analysis set title | mITT |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| All ITT patients with $\geq 10^5$ cfu/ml in the predose culture, taken at least 5 doses of medication and had the primary endpoint measurement available at Visit 3. | |
| Subject analysis set title | Sub-study group |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| The sub-cohort of patients in Singapore generated additional efficacy/pharmacokinetic data for bacterial killing rate. | |

| Reporting group values | Safety Set | mITT | Sub-study group |
|---|------------|------|-----------------|
| Number of subjects | 36 | 18 | 8 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 36 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous Units: years | | | |
| arithmetic mean | 35.9 | | |
| standard deviation | ± 12.4 | ± | ± |
| Gender categorical Units: Subjects | | | |
| Female | | | |
| Male | | | |

End points

End points reporting groups

| | |
|---|-----------------------------|
| Reporting group title | Verum |
| Reporting group description: Finafloxacin 300 mg b.i.d. for 3 days | |
| Reporting group title | Comparator |
| Reporting group description: Ciprofloxacin 250 mg b.i.d for 3 days | |
| Subject analysis set title | Safety Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Patients that received at least one dose of study medication | |
| Subject analysis set title | mITT |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: All ITT patients with $\geq 10^5$ cfu/ml in the predose culture, taken at least 5 doses of medication and had the primary endpoint measurement available at Visit 3. | |
| Subject analysis set title | Sub-study group |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: The sub-cohort of patients in Singapore generated additional efficacy/pharmacokinetic data for bacterial killing rate. | |

Primary: Efficacy - Eradication

| | |
|--|---------------------------------------|
| End point title | Efficacy - Eradication ^[1] |
| End point description: The bacteriological eradication rate of Finafloxacin when compared to Ciprofloxacin in female patients with uUTI. Defined as the eradication of initial pathogen ($\leq 10^3$ cfu/mL) in urine at Visit 3 (day 4-6) with no isolation of a new pathogen. | |
| End point type | Primary |
| End point timeframe: Days 4 - 6 after treatment start | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: With respect to the evaluation of results, no confirmatory analyses were to be performed. The original intention was to show the preliminary efficacy of Finafloxacin as a proof of concept.

| End point values | Verum | Comparator | mITT | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 28 | 8 | 36 | |
| Units: percent | | | | |
| number (not applicable) | 100 | 100 | 100 | |

Statistical analyses

No statistical analyses for this end point

Primary: Efficacy - Killing rate (2h)

| | |
|-----------------|---|
| End point title | Efficacy - Killing rate (2h) ^[2] |
|-----------------|---|

End point description:

The primary efficacy variable of the sub-study was the bacterial killing rate at 2, 4, 8, and 24 hours (in the case of patients who enrolled after 2:00 p.m. on day 1) after the first intake of study medication. Rate of bacterial killing = actual bacterial concentration / (baseline bacterial concentration * time between samplings [h]) multiplied by 10⁵

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

End point timeframe:

24 hours

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: With respect to the evaluation of results, no confirmatory analyses were to be performed. The original intention was to show the preliminary efficacy of Finafloxacin as a proof of concept.

| End point values | Verum | Comparator | Sub-study group | |
|--------------------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 5 | 3 | 8 | |
| Units: Rate of bacterial killing | | | | |
| arithmetic mean (standard deviation) | 240 (± 537) | 45 (± 46) | 167 (± 419) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Safety

| | |
|-----------------|--------|
| End point title | Safety |
|-----------------|--------|

End point description:

Percent of subjects which reported at least one treatment emergent AE.

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

End point timeframe:

Treatment start (day 1) to day 28 - 38

| End point values | Verum | Comparator | Safety Set | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 28 | 8 | 36 | |
| Units: percent | | | | |
| number (not applicable) | 57.1 | 12.5 | 47.2 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy - Superinfection

| | |
|-----------------|---------------------------|
| End point title | Efficacy - Superinfection |
|-----------------|---------------------------|

End point description:

Superinfection: isolation of a new pathogen ($\geq 10^5$ cfu/mL) on day 2 (Visit 2) or day 4-6 (Visit 3)

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

End point timeframe:

Treatments start to day 4-6

| End point values | Verum | Comparator | mITT | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 13 | 5 | 18 | |
| Units: Patients | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment start (day 1) to day 28 - 38

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 11.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | Verum |
|-----------------------|-------|

Reporting group description:

Finafloxacin 300 mg b.i.d. for 3 days

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

Reporting group description:

Ciprofloxacin 250 mg b.i.d for 3 days

| Serious adverse events | Verum | Comparator | |
|---|---|---------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 8 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Immune system disorders | | | |
| Hypersensitivity | Additional description: Allergy (facial swelling) | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 8 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Verum | Comparator | |
|---|------------------|----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 16 / 28 (57.14%) | 1 / 8 (12.50%) | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypertension | | | |

| | | | |
|---|---------------------|--------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 0 / 8 (0.00%) 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | 0 / 8 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Reproductive system and breast disorders | | | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | 0 / 8 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | 0 / 8 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|--|---|--|
| Rhinorrhoea subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 0 / 8 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 0 / 8 (0.00%) 0 | |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | 0 / 8 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Joint swelling subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 | 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Vulvovaginal mycotic infection subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 3 / 28 (10.71%) 3 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 1 / 28 (3.57%) 1 | 1 / 8 (12.50%) 1 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 03 March 2009 | Clarification of exclusion criterion no. 13 (exclusion due to laboratory values) was added to the protocol. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported