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; continous 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 pacebo (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 ≥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 ≥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 (≤ 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 10^5

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