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An open randomised comparison of gatifloxacin versus ofloxacin for the treatment of uncomplicated enteric fever

Submission date	Recruitment status	[X] Prospectively registered
16/07/2008	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
17/07/2008	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
29/11/2013	Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
ctu01tyjan08

Study information

Scientific Title

Study objectives
We hypothesise that gatifloxacin is more effective than ofloxacin in the treatment of enteric fever.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from:
1. Oxford Tropical Medicine Research Ethics Committee (OXTREC) (UK) on the 20th June 2006 (ref: 23/08)
2. Nepalese Local Ethics Committee on the 24th June 2008

Study design
An open randomised two-way comparison trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Enteric fever (typhoid and paratyphoid fever)

Interventions
Gatifloxacin (10 mg/kg/day) once daily oral dose for 7 days versus ofloxacin (20 mg/kg/) twice daily oral dose for 7 days.

1. Prior to admission to the study:
1.1. Full history and clinical examination. In particular the following data will be documented: clinical manifestations according to a standard case record form (CRF).
1.2. Chest X-ray and other radiological investigations, including abdominal ultrasound, as clinically indicated

2. On admission to the study:
2.1. Name and address of the patient will be recorded on a detachable cover sheet of the CRF, (for mapping purposes)
2.2. Full blood counts including white cell differential, biochemistry (serum glutamic oxaloacetic transaminase [SGOT], serum glutamic pyruvic transaminase [SGPT], creatinine, glucose)
2.3. Blood for on-going host genetic studies of enteric fever from the patient
2.4. Microbiology:
2.4.1. Blood cultures (5 - 8 ml of blood)
2.4.2. Stool culture pre-treatment
2.5. Blood for typhoid diagnostic study (2 ml ethylenediaminetetraacetic acid [EDTA] blood)

3. Day 1 - Discharge:
Patients will be managed as outpatients and seen at home every day to day 10 or longer (until the patient gets better). The Nurse/Dr/Paramedic will visit the patient twice per day (at 12

hourly intervals) for 10 days or longer (until the patient gets better).
3.1. Treatment will be given under directly observed therapy
3.2. GPS mapping of patient's house
3.3. Axillary temperature will be recorded at 12 hourly intervals
3.4. Random glucose monitoring, daily from day 1 till day 8
3.5. Blood for pharmacokinetic study (2 ml of blood, sparse sampling, either one blood sample or two blood samples after the third dose of gatifloxacin or ofloxacin)

At all visits fever and clinical symptoms will be monitored (feeling better or not, fever, headache, anorexia, pain abdomen, cough, constipation, diarrhoea, vomiting, nausea, confusion, black stool, sweating/dizziness, fainting/blackouts, nocturia/polyuria or others) and recorded with particular attention to:
3.6. Any side effects of the drug
3.7. Complications of the disease (if any occur)

4. Day 8:
4.1. Patients will be re-examined by the study physicians at Patan Hospital
4.2. Blood cultures will be performed day 8
4.3. Full blood counts including white cell differential, biochemistry (SGOT, SGPT, creatinine) will be repeated
4.4. Faeces will be re-cultured day 8
4.5. Blood for typhoid diagnostic study (2 ml)

5. Day 15:
All patients will be re-examined by the study physicians at Patan Hospital.

Further follow up will be performed for six months.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Gatifloxacin, ofloxacin

Primary outcome(s)
The overall failure of the treatment. Overall failure of treatment is defined as the occurrence of any one of the following (acute treatment failure plus complication plus relapse):
1. Persistent fever at day 10 of treatment
2. Blood culture positive at day 10 of treatment
3. Need for 'rescue' treatment with ceftriaxone
4. Culture confirmed relapse within 28 days of starting therapy
5. The development of any typhoid fever related complications during treatment:
5.1. Clinically significant bleeding
5.2. Fall in the Glasgow Coma Score
5.3. Perforation of the gastrointestinal tract
5.4. Admission to hospital within 28 days of starting therapy

Key secondary outcome(s))

1. Fever clearance time (FCT)
2. Syndromic clinical relapse occurring within 28 days of starting therapy that is thought to be due to typhoid or paratyphoid fever (fever, abdominal pain, change in bowel habit, headache, etc), blood cultures negative and no other cause identified
3. Stool carriage of Salmonella typhi or S. paratyphi at 1, 3, or 6 months

Completion date
31/07/2010

Eligibility

Key inclusion criteria
1. Patients give fully informed consent
2. Aged above 2 years and weigh more than 10 kg, either sex
3. Patients with fever for more than 3 days
4. Patients have no signs of severe typhoid fever, are not obtunded or shocked, are not visibly jaundiced and have no signs of gastrointestinal bleeding or any other evidence of severity
5. No previous history of hypersensitivity to either of the trial drugs
6. No known previous treatment with a fluoroquinolone antibiotic or third generation cephalosporin or macrolide within one week of hospital admission (patients who have received chloramphenicol, ampicillin, or co-trimoxazole will be included as long as they have not shown evidence of clinical response)
7. Patients are not pregnant or breast-feeding

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Not Specified

Sex
All

Key exclusion criteria
Does not comply with the above inclusion criteria

Date of first enrolment
01/08/2008

Date of final enrolment
31/07/2010

Locations

Countries of recruitment
Nepal

Viet Nam

Study participating centre
The Oxford University Clinical Research Unit (OUCRU)
Ho Chi Minh City
Viet Nam
Q5

Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
The Wellcome Trust (UK) (grant ref: 077078)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	31/10/2013		Yes	No