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A randomised comparison of ciprofloxacin, levofloxacin and gatifloxacin for the treatment of adults with tuberculous meningitis

Submission date	Recruitment status	[_] Prospectively registered
22/07/2005	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/07/2005	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
06/02/2015	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
061330

Study information

Scientific Title

A randomised comparison of ciprofloxacin, levofloxacin and gatifloxacin for the treatment of adults with tuberculous meningitis

Acronym
BN study

Study objectives
Fluoroquinolones are bactericidal for Mycobacterium tuberculosis and are recommended by the World Health Organisation (WHO) for the treatment of multi-drug resistant pulmonary tuberculosis. Reports of their use in Tuberculous Meningitis (TBM) are restricted to case reports, and there are no controlled trials to clarify their role in management. In particular, data regarding Cerebrospinal Fluid (CSF) penetration and pharmacokinetics are scant, and it is uncertain which of the fluoroquinolones represents the best drug for treating TBM.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Tuberculous meningitis

Interventions
Adults entering the study will be randomised to one of four treatment arms:
1. Conventional four drug Anti-Tuberculosis Chemotherapy (ATC) (comprising of isoniazid, rifampicin, pyrazinamide and ethambutol)
2. Conventional four drug ATC plus ciprofloxcin
3. Conventional four drug ATC plus levofloxacin
4. Conventional four drug ATC plus gatifloxacin.

The trial will be open-label. Sparse pharmacokinetic data will be generated from routine serial sampling of CSF/plasma performed upon each patient for the purposes of assessing response to treatment. Paired blood and CSF samples (for drug measurement and killing curves) will be taken at diagnosis, day two, day seven, day 30, and day 60. The precise timing of the Lumbar Puncture (LP), in relation to drug administration, will be randomised. Likewise, the timing of two further specimens of plasma (taken either side of the LP) will also be randomised.

Intervention Type
Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)
Conventional four drug anti-tuberculosis chemotherapy (comprising of isoniazid, rifampicin, pyrazinamide and ethambutol), ciprofloxcin, levofloxacin and gatifloxacin.

Primary outcome(s)
1. Clinical methods: the following will be used as markers of clinical response:
a. fever clearance, coma clearance, date of discharge, death at two months, disability or death at nine months
b. CSF pressure, lactate, white cell count, protein and glucose
2. Microbiological methods: we will attempt to demonstrate microbiological activity by two methods:
a. time to CSF sterility - serial lumbar punctures will allow us to assess the time taken to kill TBM in the CSF. 60% of adults with TBM isolated from the CSF before treatment have a sterile CSF after 48 hours of treatment, and 5% (often with resistant organisms) have TBM cultured from the CSF after 30 days of treatment (unpublished data from HTD). We aim to compare time to CSF sterility in the four treatment arms
b. time to negative CSF amplified TBM direct test (Mycobacterium Tuberculosis Direct [MTD] test: Gen-probe, California). Using the same principles described above, we will compare time to negative MTD in the four treatment arms

Key secondary outcome(s))
No secondary outcome measures

Completion date
01/02/2005

Eligibility

Key inclusion criteria
1. Aged over 14 years
2. Clinical diagnosis of TBM

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Patients who are less than 15 years old
2. Patients who are pregnant or breast feeding
3. Patients in whom the physician believes fluoroquinolones are contraindicated e.g. previous

adverse reaction
4. The consent of either the patient or their relatives is not obtained

Date of first enrolment
01/04/2003

Date of final enrolment
01/09/2004

Locations

Countries of recruitment
Viet Nam

Study participating centre
Oxford University Clinical Research Unit
Ho Chi Minh City
Viet Nam
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Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype

International organizations

Location
United Kingdom

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	01/07/2011		Yes	No