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Combination anti-fungal therapy in cryptococcal 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
05/04/2013	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
061330

Study information

Scientific Title
A randomised controlled trial of combination anti-fungal therapy in cryptococcal meningitis

Acronym
BK Study

Study objectives
Cryptococcal meningitis is the second leading cause of death in Human Immunodeficiency Virus (HIV) patients worldwide after Tuberculosis (TB). The Hospital for Tropical Diseases has seen a dramatic increase in the number of cases of cryptococcal meningitis as the HIV epidemic has accelerated in Viet Nam. The mortality rate is high, even with treatment according to international guidelines. Optimum treatment for cryptococcal meningitis is not determined. Combination treatment with amphotericin and flucytosine has shown no clinical benefit when compared with amphotericin alone, yet this combination of potentially toxic drugs has become the standard of care, recommended in US and European guidelines.

The azole drugs, with their ease of administration and good safety profile, have not been investigated in combination with amphotericin in the treatment of cryptococcal meningitis. The trial will determine whether amphotericin combined with high dose fluconazole is superior to amphotericin alone or amphotericin combined with flucytosine, using clinical endpoints.

As of 18/03/2009 the anticipated trial dates of this record have been updated; the intial trial dates at the time of registration were:
Initial anticipated start date: 01/04/2004
Initial anticipated end date: 01/01/2006

Ethics approval required
Old ethics approval format

Ethics approval(s)
The ethical review board of the Hospital for Tropical Diseases, Ho Chi Minh City, and Liverpool School of Tropical Medicine, UK gave approval prior to participant recruitment.

Study design
Open label randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Treatment Group 1:
Induction Treatment: Amphotericin 1 mg/kg/day for 4 weeks
Consolidation Treatment: Fluconazole 400 mg/day for 6 weeks
Secondary Prophylaxis: Fluconazole 200 mg/day

Treatment Group 2:
Induction Treatment: Amphotericin 1 mg/kg/day plus flucytosine 100 mg/kg/day for 2 weeks
Consolidation Treatment: Fluconazole 400 mg/day for 8 weeks
Secondary Prophylaxis: Fluconazole 200 mg/day

Treatment Group 3:
Induction Treatment: Amphotericin 1 mg/kg/day plus Fluconazole 800 mg/day for 2 weeks
Consolidation Treatment: Fluconazole 400 mg/day for 8 weeks
Secondary Prophylaxis: Fluconazole 200 mg/day

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Fluconazole, amphotericin and flucytosine

Primary outcome(s)
Mortality at 2 and 10 weeks

Key secondary outcome(s))
Amended as of 19/03/2009:
1. Rates of disability at 10 weeks
2. Rates of clearance of yeasts from CSF at 6 months
3. Changes in immune parameters at 6 months
4. Combined death and disability at 6 months
5. Death at 6 months

Initial information at the time of registration:
1. Duration of ventilation
2. Duration of supplemental oxygen
3. Duration of hospitalisation
4. Viral load in clinical specimens
5. Cytokine levels
6. Adverse effects

Completion date
01/12/2009

Eligibility

Key inclusion criteria
1. Patients aged 15 years and older
2. HIV positive
3. Cryptococcal meningitis defined by a clinical syndrome consistent with cryptococcal meningitis and one or more of: positive Cerebrospinal Fluid (CSF) culture, positive cryptococcal antigen in CSF, positive CSF india ink test

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Pregnancy
2. Renal or liver failure
3. Active TB
4. Aged less than 15 years old

Date of first enrolment
22/04/2004

Date of final enrolment
01/12/2009

Locations

Countries of recruitment
Viet Nam

Study participating centre
Hospital for Tropical Diseases
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
The Wellcome Trust (UK) (grant ref: 061330)

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	04/04/2013		Yes	No