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

Contact name

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Contact details

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

Participant information sheet

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 measure

Mortality at 2 and 10 weeks

Secondary outcome measures

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

Overall study start date

22/04/2004

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

Age group

Adult

Sex

Both

Target number of participants

300 (237 as of March 2009)

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)

Sponsor details

University Offices Wellington Square Oxford England United Kingdom OX1 2JD

Sponsor type

University/education

Website

http://www.ox.ac.uk

ROR

https://ror.org/052gg0110

Funder(s)

Funder type

Charity

Funder Name

The Wellcome Trust (UK) (grant ref: 061330)

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output typeDetailsDate createdDate addedPeer reviewed?Patient-facing?Results articleresults04/04/2013YesNo