High dose amphotericin B with flucytosine, and amphotericin B plus high dose fluconazole for treatment of cryptococcal meningitis in human immunodeficiency (HIV)-infected patients

Submission date	Recruitment status No longer recruiting	Prospectively registered		
30/09/2005		☐ Protocol		
Registration date 08/02/2006	Overall study status Completed Condition category	Statistical analysis plan		
		[X] Results		
Last Edited		Individual participant data		
21/03/2013	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

Study information

Scientific Title

Early fungicidal activity of high dose amphotericin B combined with flucytosine, liposomal amphotericin B with flucytosine, amphotericin B and high dose fluconazole compared with standard amphotericin B and flucytosine for the initial treatment of human immunodeficiency virus associated cryptococcal meningitis

Study objectives

Higher doses of amphotericin B and of fluconazole are associated with more rapid clearance of infection.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethical approval was obtained from:

- 1. REC Faculty of Health Sciences, University of Cape Town on 05/04/2004
- 2. Wandsworth LREC, London on 03/05/2005
- 3. Ethical Review Committee, Ministry of Public Health, Thailand on 02/09/2005

Study design

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

Step 1: high dose amphotericin B (1 mg/kg/day) plus flucytosine versus standard dose amphotericin B (0.7 mg/kg/day) plus flucytosine, for initial therapy. Substudy step 1: high dose liposomal amphotericin B (10 mg/kg/day) plus flucytosine will be compared to high dose amphotericin B (1 mg/kg/day) plus flucytosine.

Step 2: the optimal dose of amphotericin (from the first step) will be combined with 800 mg/day of fluconazole, or 1200 mg/day of fluconazole compared with the standard regimen of amphotericin B plus flucytosine.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

High dose amphotericin B, flucytosine, amphotericin B, high dose fluconazole, flucytosine

Primary outcome measure

Early fungicidal activity (EFA) of alternative regimens based on serial quantitative CSF cultures over the first two weeks of therapy.

Secondary outcome measures

- 1. Clinical and laboratory side effects
- 2. Mortality and morbidity at ten weeks

Overall study start date

01/06/2005

Completion date

01/06/2007

Eligibility

Key inclusion criteria

- 1. 18 years old or more, either sex
- 2. Human immunodeficiency virus (HIV) seropositive
- 3. First episode of cryptococcal meningitis on basis of positive cerebrospinal fluid (CSF) India ink or CSF cryptococcal antigen

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

150

Key exclusion criteria

- 1. Liver function test alanine aminotransferase (ALT) formerly known as serum glutamate pyruvate transaminase (SGPT) greater than five times upper limit of normal
- 2. Absolute neutrophil count less than 500 x 10^6/l
- 3. Platelets less than $50,000 \times 10^6/l^3$
- 4. Creatinine greater than 2.5 mg/dl^4
- 5. Pregnant or lactating women
- 6. Previous serious reaction to any of the study drugs
- 7. Currently taking systemic antifungal therapy

Date of first enrolment

01/06/2005

Date of final enrolment

01/06/2007

Locations

Countries of recruitment

South Africa

Thailand

United Kingdom

Study participating centre Department of Infectious Diseases

London United Kingdom SW17 ORE

Sponsor information

Organisation

St. George's Medical School (UK)

Sponsor details

Cranmer Terrace London United Kingdom SW17 ORE

Sponsor type

University/education

Website

http://www.sgul.ac.uk/

ROR

https://ror.org/040f08y74

Funder(s)

Funder type

University/education

Funder Name

British Infection Society (UK)

Alternative Name(s)

BIS

Funding Body Type

Private sector organisation

Funding Body Subtype

Associations and societies (private and public)

Location

United Kingdom

Funder Name

Trustees of St. Georges Hospital, University of London (UK)

Funder Name

The Wellcome Trust (UK) (grant ref: 052199)

Funder Name

Medical Research Council (MRC) (UK) (grant ref: G0501476)

Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

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 type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2008		Yes	No