

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 30/09/2005	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 08/02/2006	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 21/03/2013	Condition category Infections and Infestations	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Thomas Harrison

Contact details
Department of Infectious Diseases
St. George's Medical School
Cranmer Terrace
London
United Kingdom
SW17 0RE

Additional identifiers

Protocol serial number
N/A

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

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

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 $500 \times 10^6/l$
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

United Kingdom

South Africa

Thailand

Study participating centre

Department of Infectious Diseases

London

United Kingdom

SW17 ORE

Sponsor information

Organisation

St. George's Medical School (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, Medical Research Committee and Advisory Council, MRC

Funding Body Type

Government organisation

Funding Body Subtype

National government

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	01/07/2008		Yes	No