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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	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 08/02/2006	**Overall study status** Completed	
Last Edited 21/03/2013	**Condition category** 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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

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 x 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