

# High dose fluconazole with or without flucytosine in the treatment of human immunodeficiency virus (HIV)-associated cryptococcal meningitis

<b>Submission date</b> 11/02/2008	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 20/03/2008	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 05/01/2010	<b>Condition category</b> 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**  
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## Additional identifiers

**Protocol serial number**  
MRC (UK) ref: 76201; 1.0

## Study information

**Scientific Title**

A randomised controlled clinical trial to evaluate high dose fluconazole with or without flucytosine in the treatment of human immunodeficiency virus (HIV)-associated cryptococcal meningitis

### **Study objectives**

As of 27/02/2009 this record was updated to include the second phase Step 2 within this record. Ethics approval was extended to include this phase. All additions to this record regarding Step 2 can be found in the relevant field under the title Step 2. The titles for Step 2 are as follows:  
Step 2 public title: High dose fluconazole with short course amphotericin B, with or without flucytosine in the treatment of human immunodeficiency virus (HIV)-associated cryptococcal meningitis

Step 2 scientific title: A randomised controlled clinical trial to evaluate high dose fluconazole with short course amphotericin B, with or without flucytosine in the treatment of human immunodeficiency virus (HIV)-associated cryptococcal meningitis

Please also note that the anticipated start and end dates for Step 2 are as follows:

Step 2 anticipated start date: 01/03/2009

Step 2 anticipated end date: 01/01/2010

At the time of registration, the initial trial dates reflected Step 1 of this trial, and therefore these have been amended to include the Step 2 dates as above; the initial end date (for Step 1) was 18/02/2009.

Step 1 hypothesis:

Addition of flucytosine to fluconazole will lead to more rapid sterilisation of cerebrospinal fluid (CSF) in cryptococcal meningitis.

Step 2 hypotheses:

1. In the presence of a short course of amphotericin B, the addition of flucytosine to fluconazole (1200 mg/d) will lead to more rapid sterilisation of cerebrospinal fluid (CSF) in cryptococcal meningitis
2. A short course of amphotericin B will avoid toxicity observed in longer courses of amphotericin B.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

1. Malawi National Health Sciences Research Committee approved on the 8th November 2007 (Step 2 amendment: 17th February 2009)
2. Wandsworth LREC (covering St Georges University of London UK) approved on the 8th January 2008 (Step 2 amendment: 13th February 2009)
3. Institutional review board (IRB) University of North Carolina at Chapel Hill approved on the 29th November 2007 (Step 2 amendment pending as of 26/02/2009)

### **Study design**

Randomised open-labelled controlled trial

### **Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Cryptococcal meningitis/ HIV

**Interventions**

Step 1:

1. Fluconazole 1,200 mg/d for two weeks
  2. Fluconazole 1,200 mg/d plus flucytosine 100 mg/kg/d for two weeks
- After two weeks all patients receive fluconazole 800 mg/d.

Step 2:

1. Amphotericin B 1 mg/kg daily for 7 days plus fluconazole 1200 mg/d (started concurrently) for 2 weeks
  2. Amphotericin B 1 mg/kg daily for 7 days, plus fluconazole 1200 mg/d, plus flucytosine 100 mg/kg/day (started concurrently) for 2 weeks
- After two weeks all patients receive fluconazole 800 mg/d.

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Fluconazole, flucytosine

**Primary outcome(s)**

Early fungicidal activity (rate of clearance of infection) of alternative regimens over the first two weeks of therapy.

**Key secondary outcome(s)**

1. Clinical and laboratory side effects
2. Mortality at 2 and 10 weeks

**Completion date**

01/01/2010

**Eligibility****Key inclusion criteria**

1. Patients greater than 18 years, either sex
2. A first episode of cryptococcal meningitis

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Key exclusion criteria**

1. Alanine aminotransferase (ALT) greater than five times the upper limit of normal
2. Pregnancy or lactation
3. Previous serious reaction to study drugs
4. Taking systemic anti-fungals
5. Polymorphonuclear leukocytes (PMNs) less than  $500 \times 10^6/L$
6. Platelets less than  $50,000 \times 10^6/L$
7. Concomitant medication that is contraindicated with any study drugs
8. Already on antiretroviral therapy (ART)

STEP 2 additional criteria:

9. Initial creatinine greater than 2.5 mg/dl

**Date of first enrolment**

18/02/2008

**Date of final enrolment**

01/01/2010

**Locations****Countries of recruitment**

United Kingdom

Malawi

**Study participating centre**

**Cranmer Terrace**

London

United Kingdom

SW17 ORE

**Sponsor information****Organisation**

St George's University of London (UK)

**ROR**

<https://ror.org/040f08y74>

## Funder(s)

### Funder type

Research council

### Funder Name

Medical Research Council (UK) (grant ID: 76201)

### 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?
<a href="#">Results article</a>	results	01/02/2010		Yes	No