

PATIENT SCREENING

Please also refer to the related WPD

Any **HIV-infected** patient ≥ 18 years old,
with confirmed **1st episode of CM:**

Positive CSF CrAg
and/or **positive CSF India ink**
and/or positive CSF culture

Confirm **HIV positive status**
(Clinical history or HIV test)

Exclude lactation & pregnancy
for all women
(Urinary or Serum test)

And screen for all exclusion criteria

Invite patient to enter study
and obtain **INFORMED CONSENT**

RANDOMISATION

Perform **Day 1 LP:**
Measure **CSF opening pressure**
+
CSF volumes and investigations as per study protocol
& **baseline blood tests** as per study protocol

Treat as per protocol arm

SINGLE DOSE ARM

Liposomal Amphotericin B
Ambisome
10mg/kg (Day 1 only)
+
Fluconazole 1200mg/day
for 14 days (Day 1-14)
+
Flucytosine 100mg/kg/day
for 14 days (Day 1-14)

CONTROL ARM

Amphotericin B deoxycholate
1mg/kg/day for 7 days (Day 1-7)
+
Flucytosine 100mg/kg/day
for 7 days (Day 1-7)

THEN

Fluconazole 1200mg/day
for 7 days (Day 8-14)

EXCLUSION CRITERIA

- 1. Pregnancy or lactation**
- 2. Previous serious reaction to study drugs**
- 3. Already taking antifungal treatment at CM treatment doses:**
 - o Amphotericin B ≥ 0.7 mg/kg for > 48 hrs
 - o or Fluconazole ≥ 800 mg/day for > 48 hrs
- 4. Concomitant medication contraindicated with study drugs:**
 - o terfenadine, cisapride, pimozide, astemizole, quinidine and erythromycin (with Fluconazole)
 - o cytarabine (with Flucytosine)
- 5. HIV negative**



EARLY WITHDRAWAL CRITERIA On baseline blood testing:

1. ALT > 5 times upper limit of normal (i.e. > 200 IU/ml)
2. PMNs < $500 \times 10^6/L$
3. Platelets < $50,000 \times 10^6/L$