

RANDOMISATION

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)

MANAGEMENT of RAISED INTRACRANIAL PRESSURE

Please also refer to the related WPD

Raised intra-cranial pressure (ICP) is associated with worse symptoms, including:
headache, nausea, diplopia secondary to sixth cranial nerve palsies, and **altered mental status**.

Repeated daily therapeutic lumbar punctures (LP) are sufficient to control raised pressure in the majority of patients.

Identify CSF opening pressure (OP) at baseline LP

A prompt baseline lumbar puncture is strongly encouraged,
but in the presence of **focal neurologic signs**, excluding sixth (VIth) cranial nerve palsies,
it should be delayed pending the results of a computed tomography (CT) or magnetic resonance imaging (MRI) scan, if available.

If CSF OP is ≥ 30 cm H₂O, remove CSF (therapeutic LP)

If OP 20-30, therapeutic LPs are at the discretion of the study doctor who will be guided by patient symptoms

Reduce OP by 50% if OP very high
or to a normal pressure of **< 20 cm H₂O**

Do not remove more than 40 ml of CSF
at any therapeutic LP

The CSF OP should be rechecked after
removal of **every 10mL CSF**.

If the preceding day, OP was ≥ 30 cm H₂O, **repeat daily LP to evaluate OP**
If OP was 20-30, therapeutic LPs **guided by symptoms and signs of raised ICP**

Perform **daily therapeutic LP** until the CSF pressure and symptoms have been **stabilized for > 2 days**

Consider temporary percutaneous lumbar drains or ventriculostomy, if over 14 daily LPs required to control OP

NB This requires significant monitoring and is an infection risk,
therefore should only be contemplated if sufficient resources are available for managing a lumbar drain

Patients admitted to the study, regardless of their initial opening pressure,
will undergo serial lumbar punctures on **days 1, 7 and 14** of their admission.
The opening pressure must be measured and documented for each and every lumbar puncture.

Mannitol has no proven benefit and is not recommended.
Acetazolamide should be avoided to control increased intracranial pressure.
Corticosteroids should not routinely be used during induction therapy for HIV-associated cryptococcal meningitis.