Single-Dose Liposomal Amphotericin B for Cryptococcal Meningitis in Low-Resource Settings

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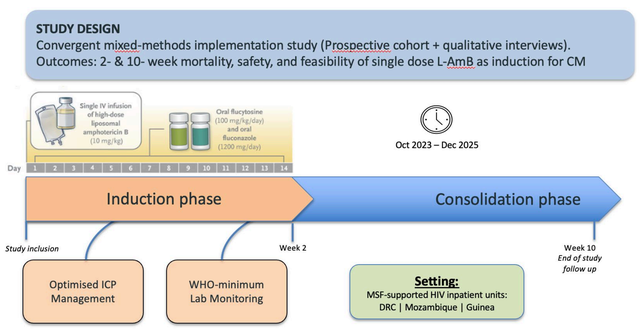
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BACKGROUND

- Cryptococcal meningitis (CM) remains **the second leading cause of AIDS-related mortality after tuberculosis**.
- In 2022, the World Health Organization recommended a single high-dose liposomal amphotericin B (L-AmB) regimen with fluconazole and flucytosine as induction therapy for cryptococcal meningitis.
- This was based on the **AMBITION-cm trial** which showed 2-week and 10-week mortality of 13% and 24% with reduced toxicity in comparison to 7 days of conventional amphotericin B.
- Data from implementation of this regimen as part of routine care in low-resource settings remain limited..

METHODS

Methodology: Study Design and Treatment Pathway



- **Adults (≥18 years) with HIV-associated cryptococcal meningitis** received a single 10 mg/kg L-AmB infusion plus 14 days of oral fluconazole and flucytosine with standardized intracranial pressure (ICP) management and WHO-minimum laboratory monitoring.
- **Fidelity** to recommended management was assessed.
- **Outcomes**: Mortality at 2- and 10-weeks.

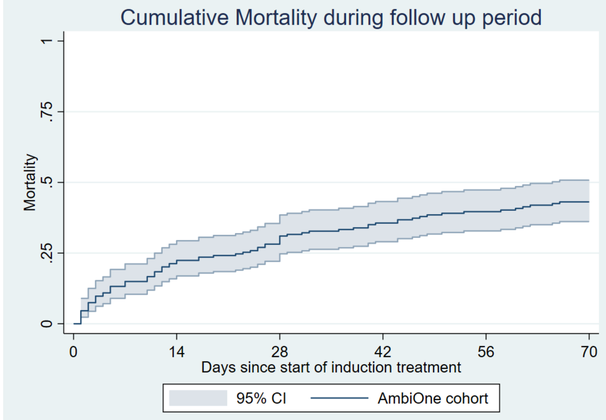
The single-dose L-AmB regimen implemented in low-resource hospital settings in Guinea, DRC and Mozambique simplified inpatient care, enabled early discharge in 37% of participants and was acceptable to healthcare workers.

RESULTS

- **174 participants** were eligible from 195 screened (October 2023 – December 2025)
- Baseline characteristics are shown in table 1.

Primary outcomes

- **Two-week mortality was 22%** [39/174 (95 CI 17-30)]
- **Ten-week mortality was 43%** [70 /174 (95 CI 36-51)].
- Lost to follow up was <1% (1/174).



Time (days)	N at risk	Mortality % (95% CI)
1	174	4.6 (2.3–9.0)
14	137	22.4 (16.9–29.4)
28	125	31.0 (24.7–38.5)
42	113	35.6 (29.0–43.2)
56	106	39.7 (32.8–47.3)
70	99	43.1 (36.1–50.8)

Figure 1: Kaplan Meier Survival Graph with 95% confidence interval and risk tables.

Adverse events

- Grade III/IV renal impairment: 2% (4/174)
- Grade III/IV hypokalaemia: 3% (5/174)
- Mean haemoglobin decline of 1.5 g/dL (from 10.2 to 8.7) by day 7.

Favourable toxicity profile compared to 7 days of conventional amphotericin B deoxycholate.

Table 1: Baseline characteristics of AmbiOne cohort

Characteristic	Overall (N=174)	Guinea (n=51)	DRC (n= 91)	Mozambique (n= 32)
Age, years (IQR)	40 (32-48)	40 (32-45)	40 (33-49)	39 (30-45)
Female sex, % (n/N)	49 (86/174)	41 (21/51)	58 (53/91)	39 (12/32)
Median CD4 count* (cells/µL) (IQR) *30 missing data due to CD4 stockout or VISITECT use	50 (35 – 122)	49 (24-70)	68 (36-126)	58 (40-118)
ART experienced at admission* % (n/N) * 3 missing data	62 (106/171)	53 (27/51)	66(58/88)	66 (21/32)
GCS score <15 %(n/N)	41 (72/174)	43 (22/51)	43 (39/91)	34 (11/32)
Opening pressure (>25cm %)** >19cm (%) as per adjustment for use of infusion line as measuring device **26 missing data	37 (55/148) 50 (71/143)	16 (8/49) 27 (13/49)	40 (32/80) 54 (43/80)	79 (15/19) 79 (11/14)

Implementation fidelity

Table 2: Fidelity to WHO minimum care package and duration of stay outcomes

Implementation indicator	Measure	Aim
Time from admission to treatment <4hrs	**85%** (148/174) DRC 92% Guinea 94%, Mozambique 50%^	100% *^In the DRC and Guinea CrAg was performed POC and AmpB & LP kits were co-located in the triage area. In Mozambique hospital policy restricted CrAg testing to the laboratory site.*
LP compliance *(Baseline OP measured with at least one further opening pressure measured during admission)*	**79%** (138/174) DRC: 80% Guinea: 94% Mozambique: 50%	100%
Complete compliance with blood test schedule *(K & Cr: D3, FBC: D7)*	**34%** (59/174) DRC: 32% Guinea: 57%, Mozambique 3%	>80%
Median length of admission *(those that died in hospital excluded)*	**8 days (5-14)** DRC: 7 (4-12) Guinea: 9 (6-13) Mozambique: 14 (7-22)	Historical comparator: 11 days (8 -14) DRC 7 (5 – 9) Guinea 12 (7-14) Mozambique: 12 (10-16)
Median time to death	**14 (4-32)** DRC: 14 (5-28) Guinea: 13 (3-28) Mozambique: 28 (1-47)	

Early discharge

- **37% (49/133) of those that survived to discharge were discharged prior to day 7** [DRC: 48% (33/69), Guinea: 32% (12/38), Mozambique:15% (4/26)]
- Amongst those discharged, **raised intracranial pressure was identified in 14%** (18/133) after discharge.

Qualitative findings

Semi-structured interviews were conducted with 37 healthcare workers across the 3 study sites.

High acceptability - a regimen more compatible with resource limited healthcare systems:

- Nurses: Marked reduction in burden of IV administration work due to fewer amphotericin B infusions
- Doctors: Perceived reductions in length of stay and laboratory monitoring requirements in comparison to conventional Amp B.

System level challenges in cryptococcal care that regimen simplification does not address:

- Late referral from other services.
- Performance of lumbar puncture a significant barrier in non-specialist centres.
- Cost to participants is a significant barrier to post discharge care.

"Sometimes the family has to decide if they want to pay for a readmission or for a funeral"

Key implementation lessons

- Co-location of LP kits, CrAg tests, and L-AmB at the triage area reduced time to treatment.
- Early discharge requires structured ICP surveillance.
- Infusion-line ICP measurement requires adjusted treatment thresholds.

CONCLUSIONS

- Single-dose L-AmB was **feasible to implement outside of controlled research settings with acceptable early outcomes and low toxicity**.
- 37% were discharged before day 7, **reducing inpatient burden**.
- However, **substantial mortality between weeks 2 and 10, largely post-discharge**, indicates that regimen simplification must be paired with strengthened follow-up and ICP surveillance to sustain gains post-hospitalisation.

PLAIN LANGUAGE SUMMARY

A one-off intravenous dose of antifungal treatment for cryptococcal meningitis was introduced in three low resource healthcare systems. It simplified treatment and reduced time in hospital. However, many patients died after discharge, showing that increased follow-up and monitoring is needed.

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