

## RESEARCH SUMMARY

# Single-Dose Liposomal Amphotericin B Treatment for Cryptococcal Meningitis

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## CLINICAL PROBLEM

Cryptococcal meningitis is the second leading cause of human immunodeficiency virus (HIV)-related death worldwide. For first-line treatment, the World Health Organization (WHO) recommends induction therapy with a 1-week regimen of amphotericin B deoxycholate plus flucytosine, followed by fluconazole therapy. However, amphotericin B deoxycholate carries the risk of substantial toxic effects; thus, the development of safer therapeutic alternatives is warranted.

## CLINICAL TRIAL

**Design:** A phase 3 open-label, randomized, controlled trial examined whether induction therapy with a single dose of liposomal amphotericin B plus flucytosine and fluconazole would be noninferior to the standard WHO-recommended first-line treatment for cryptococcal meningitis.

**Intervention:** 844 HIV-positive adults with cryptococcal meningitis residing in sub-Saharan Africa were randomly assigned to receive a single high dose of liposomal amphotericin B (10 mg per kilogram of body weight) plus 14 days of flucytosine and fluconazole or to receive standard care with 7 days of amphotericin B deoxycholate (1 mg per kilogram per day) plus flucytosine, followed by 7 days of fluconazole. The primary end point was death from any cause at 10 weeks after randomization.

## RESULTS

**Efficacy:** The single-dose liposomal amphotericin B regimen was noninferior to the standard regimen with respect to death from any cause at 10 weeks.

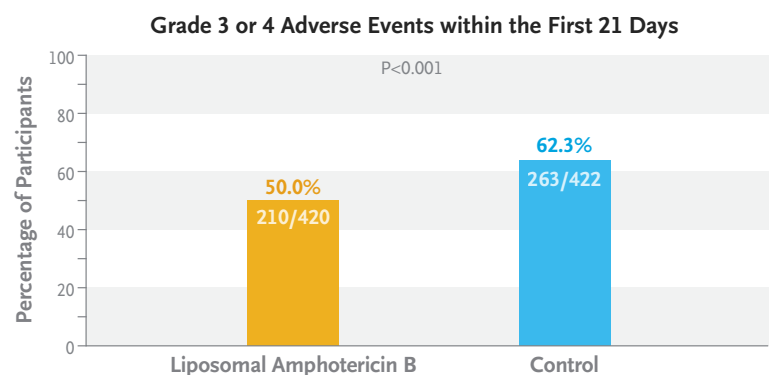
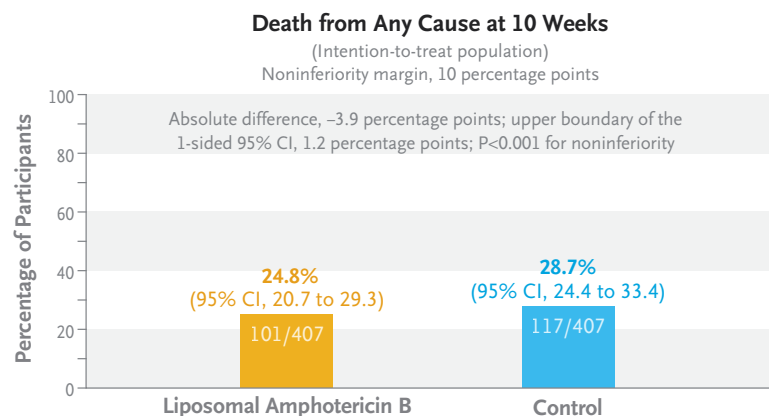
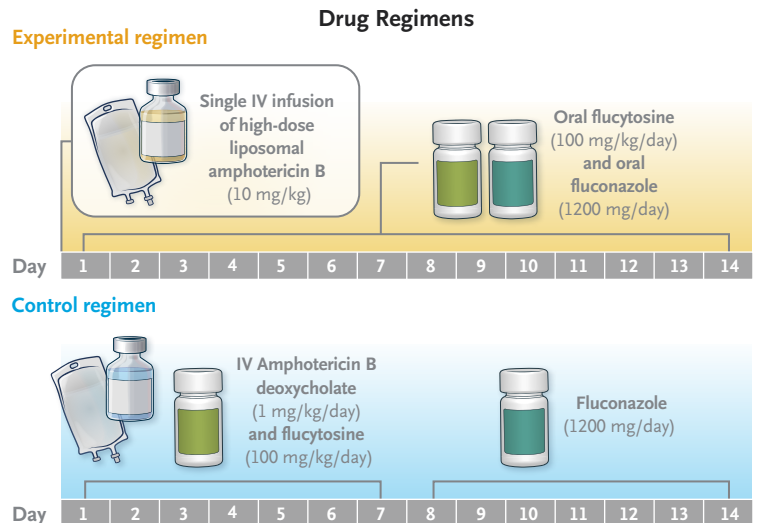
**Safety:** The incidence of grade 3 or 4 adverse events within the first 21 days of treatment was significantly lower with the single-dose liposomal amphotericin B regimen than with standard care.

## LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

- Whether the single-dose liposomal amphotericin B regimen would allow for shorter hospital stays and be cost-effective in real-world settings.
- Whether other fungal infections, such as histoplasmosis and talaromycosis, could be treated with the single-dose liposomal amphotericin B regimen.

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## CONCLUSIONS

Among HIV-positive adults with cryptococcal meningitis, a single high-dose infusion of liposomal amphotericin B plus oral therapy with flucytosine and fluconazole was noninferior to the standard treatment and was associated with fewer adverse events.