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Cryptococcal meningitis treatment and diagnosis

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HIV-associated cryptococcal meningitis (CM) is now the commonest form of adult meningitis in southern, east, and central Africa, and a major contributor to HIV-associated morbidity and mortality, causing an estimated 181,000 deaths worldwide each year accounting for approximately 15% of all HIV-related mortality. Despite widespread roll-out of antiretroviral therapy (ART), the number of cases of CM has remained relatively stable in many African countries as an increasing population of patients discontinuing or failing ART offsets any decline in the number of patients with advanced HIV at first presentation. Current treatments for CM are inadequate. Ten-week mortality is approximately 60% with fluconazole treatment, the current standard-of-care in most of Africa. Conventional amphotericin B induction is more effective, but not widely available outside South Africa; use is limited by serious toxicity and the need for intensive nursing care and laboratory monitoring. New treatments are urgently needed. Recent data suggest highly effective and much safer therapy for HIV-associated CM is possible with a novel short-course of high-dose liposomal amphotericin (L-AmB, Ambisome), a newer formulation of amphotericin B. Results from our recently completed phase-II study show that a single high (10mg/kg) dose of liposomal amphotericin B is safe, and leads to rapid clearance of infection. We are currently undertaking a multi-centre phase-III randomised non-inferiority trial to determine whether short-course high-dose liposomal amphotericin B is as effective as standard amphotericin B-based therapy in averting all-cause mortality in HIV-associated CM. I will discuss the rationale for and design of the ongoing treatment trial, and discuss other recent approaches to improving outcomes in patients with CM. I will also present data from our studies in Botswana and South Africa validating novel diagnostic tests for cryptococcal infection, and exploring screening strategies to prevent patients with advanced HIV disease from developing CM.