

Liposomal Amphotericin B Targeting to Fungal Infections

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The liposomal formulation of amphotericin B, known as AmBisome, unlike other amphotericin B formulations, is composed of small, stable liposomes (<100nm) with a prolonged circulation time. Due to its small size, and extended half-life, it can penetrate into sites of inflammation and infection and bind to fungal cell walls. The fungi are then killed as the amphotericin B is released from the liposomes. In preclinical pulmonary models, such as aspergillosis and blastomycosis, and in brain infections, such as cryptococcosis, candidiasis, coccidioidomycosis and mucormycosis, high doses of AmBisome (5-15mg/kg) have reduced or cleared the fungus from the target tissues and markedly increased survival rates. In a murine systemic candidiasis model, a one week loading dose of AmBisome at 20mg/kg every other day, followed by once weekly treatment at lower doses (2.5-10mg/kg) was effective in significantly reducing the fungal burden in the kidneys even one month after treatment was terminated. This sustained bioactivity of AmBisome has also been observed in several prophylaxis models (histoplasmosis, candidiasis, and aspergillosis) and drug concentration studies have shown that AmBisome remains in the tissues for several weeks post-treatment. With its broad spectrum of antifungal activity and markedly reduced toxicities compared to other amphotericin B formulations, new prophylactic and therapeutic regimens for using AmBisome should be explored.