Session #44: Fungal Diagnostics and Therapy
Thursday, October 18th 2012: 12:30 p.m. – 2:00 p.m.

#222. Customized Induction Therapy for the Treatment of Cryptococcal Meningitis Based on Initial Fungal Burden

Part of Session: 44. Fungal Diagnostics and Therapy

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Background: Cryptococcal meningitis (CM) has emerged as one of the most frequent and deadly opportunistic infections in HIV patients, with a global burden estimated at nearly 1 million cases annually. Substantial barriers exist in adhering to the accepted therapeutic guidelines, including costs, availability of drugs and the severe and potentially life-threatening toxicity of amphotericin. Successful induction therapy relies on finding a balance between fungal clearance and minimization of amphotericin toxicity, and patients may therefore benefit from a more customized approach to therapy. Using early fungicidal activity (EFA), or rate of fungal clearance, we examined strategies to customize the duration of induction therapy based on initial fungal burden.
Methods: Fungal burden and clearance from 133 HIV-positive ART-naïve patients enrolled in a large multi-site amphotericin-based treatment trial in Africa was analyzed. EFA was estimated by linear regression of serial quantitative cerebrospinal fluid cultures. Pooled EFA was used to estimate the time required for fungal clearance for each subject based on their initial fungal burden. Patients were grouped into theoretical 7, 10, and 14 day amphotericin induction regimens. The likelihood of clearing the infection by the end of treatment period was explored and cost analysis estimated.
Results: The EFA for 14 days of amphotericin + fluconazole 800mg/day was -0.34±0.25 log CFU/mL CSF/day, which was slightly lower than that observed using the same regimen in other trials. Most of the patients analyzed still would have required 14 days to clear infection, though many patients would have cleared their infection in 7 or 10 days. This customized approach to induction therapy for CM significantly decreased costs and hospital burden in our theoretical
model.
Conclusion: Early fungicidal activity may be a useful means to explore customized antifungal therapy for cryptococcal meningitis, such as shortened courses of induction therapy in certain patients with low initial fungal burdens. Our results support the further use of this approach in phase II studies to determine if the theoretical benefits observed translate to improvements in safety and mortality.