

<sup>1</sup>Glucose normalized, acidosis resolved, steroids tapered, etc. In the absence of optimal surgical debridement and risk factor mitigation, anti-fungal therapy has limited effectiveness.

<sup>2</sup>Although higher dose L-AmB has been used in practice for some patients, there are no data clearly demonstrating that it improves survival. But there are data suggesting high dosing of L-Amb triggers accelerated blood clearance of subsequent doses. Higher dose of lipid also leads to higher rates of complement-mediated infusion reactions. There are no data clearly demonstrating improved survival with addition of azoles or echinocandins to L-AmB. <sup>3</sup>Consider azole step-down after 1-2 weeks of L-AmB in clinical stable/improving patients. Overlap azoles with L-AmB for at least 3 days to achieve adequate levels. Adjust azole dose based on trough serum concentration and organism MIC, to optimize efficacy and avoid toxicity. Depending on organism MIC and drug, target trough concentrations range of 0.5-3mg/l is typical.

<sup>4</sup>Itraconazole has been used successfully in some patients in the past Best to confirm susceptibility with culture/MIC. Historically some effectiveness with *Rhizopus, Apophysomyces, Rhizomucor, Absidia* (Reclassified as *Lichtheimia*) and *Saksenaea, but less* effective for *Mucor* and *Cunninghamella*. Itraconazole tablets are not well absorbed. Absorption of oral solution is better, but expensive. Need to check trough drug levels.