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## ANTIFUNGAL THERAPY OF MURINE INFECTION WITH ASPERGILLUS TERREUS

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**Background:** In recent years, *Aspergillus terreus* has been an increasingly frequent pathogen in both the United States and Europe. Herein, we evaluated posaconazole (POS), amphotericin B (AMB), and caspofungin (CASPO) against *A. terreus* isolate #R-3371 in a neutropenic mouse model. **Methods:** The day before infection ICR mice were rendered neutropenic with 5-fluorouracil at 150 mg/kg intravenously (IV) and cyclophosphamide at 200 mg/kg intraperitoneally (IP). Mice were infected IV with  $2 \times 10^5$ - $1.5 \times 10^7$  conidia/mouse. MICs using the NCCLS M38-P method for POS, AMB, and CASPO respectively, at 48 hrs, were 0.06, 2, and  $<0.125$   $\mu\text{g/ml}$ . Therapy began the day after infection and continued through day 7 with POS at 10, 20, or 40 mg/kg orally daily, AMB at 6 mg/kg daily or 10 mg/kg every other day IP, or CASPO at 0.5, 5, 10, or 15 mg/kg IP daily. Control mice received water orally daily. Mice were observed through day 8 for survival. For tissue burden studies mice were treated day 1-7 and were terminated on day 8. Mice succumbing before day 8 had tissues removed for tissue burden. Spleens and lungs were removed, weighed, homogenized, and fungal burden was measured by serial semi-quantitative counts. Statistical analysis was performed using Log rank tests for survival and Mann-Whitney tests for tissue burden studies with  $p < 0.05$  for significance. **Results:** In 3 studies AMB was not effective in prolonging survival. Only at 10 mg/kg every other day was AMB effective in reducing the spleen counts lower than those of controls. CASPO at 15 mg/kg prolonged survival and reduced spleen counts, though inconsistently. The lower doses of CASPO were ineffective. POS at 40 mg/kg prolonged survival and reduced both spleen and lung burdens. POS at 20 mg/kg, but not at 10 mg/kg, prolonged survival, while both 20 and 10 mg/kg doses reduced lung, but not spleen, burdens. **Conclusion:** The new broad spectrum triazole POS may have an increasing role in treatment of AMB resistant mycelial pathogens such as *A. terreus*.