SCY-078 Demonstrates Significant Antifungal Activity in a Murine Model of Invasive Aspergillosis

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Azoles are the most common anti-fungal agents for the treatment of Aspergillus infections. Echinocandins have demonstrated utility in Aspergillus infections, but are limited in use due to a lack of oral bioavailability. SCY-078 is a novel, oral and intravenous (IV), triterpenoid glucan synthase inhibitor with activity against Aspergillus and Candida, currently in clinical development for the treatment of invasive fungal infections. This study was conducted to evaluate the in vivo antifungal activity of SCY-078 in a murine model of invasive aspergillosis (IA).

RESULTS

SCY-078 was well-tolerated at all doses. Treatment with SCY-078 at 7.5 mg/kg/day and 10 mg/kg/day BID significantly increased mean survival in all strains (P ≤ 0.003). SCY-078 also resulted in significant reductions in fungal kidney burden (p<0.05) and serum GM levels (p<0.005) in all strains. Primary and secondary efficacy endpoints were also met in the groups treated with IP administration of CSP or AMB. Plasma levels of SCY-078 ranged from ≈15-20 µM*hr (AUC0-12) with Cmax ranging from ≈ 1-1.6 µg/mL for the two dose groups.

CONCLUSION

SCY-078 demonstrated potent activity against WT and azole-resistant strains of A. fumigatus in a murine model of invasive aspergillosis. The exposure needed to achieve efficacy is in line with efficacious exposures reported in the invasive candidiasis models. These results support further development of SCY-078 as an oral treatment for IA infections.

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