SCY-247, A SECOND-GENERATION TRITERPENOID ANTIFUNGAL DEMONSTRATES BROAD TISSUE DISTRIBUTION AND EFFICACY IN MURINE FUNGAL INFECTION MODELS

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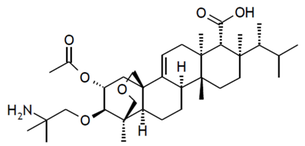
BACKGROUND



Achieving broad pharmacologically-relevant tissue distribution for antifungals remains a challenge against invasive fungal infections.

SCY-247 is a second-generation oral/IV triterpenoid antifungal in development for resistant yeasts, molds and dimorphic fungi. Here we present SCY-247 kidney, lung and epithelial lining fluid (ELF) distribution and efficacy data in two *in vivo* murine *Candida* and Mucorales infection models.

METHODS

Survival and tissue fungal burden were determined in murine efficacy models of invasive candidiasis and pulmonary mucormycosis. Neutropenic mice were infected with *C. glabrata* (~10^8 yeast cells/mouse) or *R. delemar* (2.5x10^5 spores/mouse) followed by 7 days of oral SCY-247 (16, 32 and 48 mg/kg BID). Survival and/or tissue burden, as well as SCY-247 exposure levels were assessed. Separately, rats were administered SCY-247 (20 mg/kg PO) to compare exposure in plasma, ELF, and whole lung tissue.

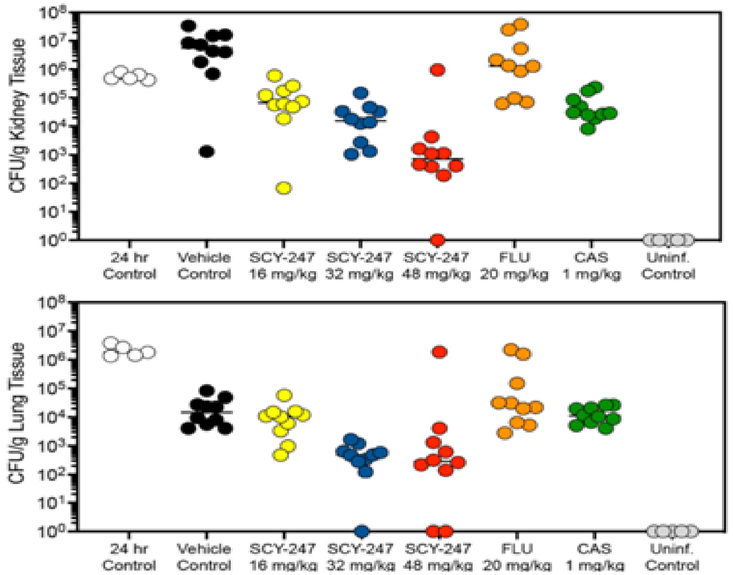
CONCLUSION

SCY-247 demonstrates excellent dose and exposure correlation with tissue penetration and reduction in fungal burden in challenging models of lung and kidney fungal infections.

RESULTS

Candida glabrata Murine Model

Figure 1: SCY-247 demonstrated significant reductions in fungal burden (p≤0.001) at all doses in kidney (top) and at 32 and 48 mg/kg in lung (bottom) in the *C. glabrata* model.



SCY-247 Tissue Distribution

Bioanalysis of samples from *C. glabrata* murine model demonstrated SCY-247 preferentially (~10X) distributed to mouse lung and kidney tissues versus plasma, and reductions in fungal burden correlated with dose and exposure. In rats, exposure in ELF and lung tissue 4 and 24 hr post-dose were ~4X and ~10X that in plasma.

Pulmonary Mucormycosis Murine Model

Figure 2: SCY-247 (32 and 48 mg/kg) resulted in prolonged survival vs placebo (p<0.05)

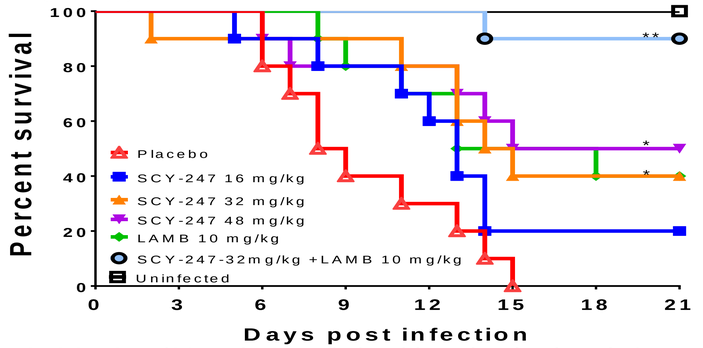


Figure 3: SCY-247 (32 and 48 mg/kg) achieved reductions in lung and brain fungal burden vs. placebo (p<0.05)