SCY-078, a Novel Intravenous and Oral Antifungal Agent, Demonstrates Extensive Tissue Distribution in Rats Following Single Intravenous Infusions and Oral Doses of [14C]SCY-078

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INTRODUCTION

- SCY-078 is an intravenous (IV) and orally (PO) bioavailable β-1,3-glucan synthesis inhibitor currently in clinical development for invasive and mucocutaneous infections caused by Candida or Aspergillus species (spp).
- Oral SCY-078 recently demonstrated clinical activity in proof-of-concept studies in invasive candidiasis as well as vulvovaginal candidiasis (VVC).
- SCY-078 inhibits fungal glucan synthesis (GSI), but is structurally distinct from other currently available GSIs (echinocandins), and demonstrates in vitro activity against both azole-resistant and the majority of echinocandin-resistant strains of Candida spp.

The objectives of this study were to characterize, following single PO or IV infused doses of [14C]SCY-078, to pigmented and non-pigmented rats, the:
1) Pharmacokinetics (PK)
2) Tissue distribution profile
3) Rate and extent of excretion

METHODS

SCY-078 is widely distributed after IV or PO dosing in rats. The concentrations in tissues, commonly affected by fungal infections (e.g., spleen, kidney, liver, lung and vagina), exceeded plasma concentrations by several fold. These results support development of SCY-078 for treating systemic and mucocutaneous fungal infections.

RESULTS

The fraction absorbed following PO administration was ~33%. SCY-078 was extensively distributed into tissues. Tissue concentration versus time indicated a rapid distribution phase over the first 8 h followed by a 24-168 h elimination phase.

The blood:tissue ratios in the organs typically associated with invasive fungal disease were as follows: spleen (54), liver (50), lung (31), bone marrow (25), kidney (20), skin (12 non-pigmented, 18 pigmented), vaginal tissue (9) and skeletal muscle (4).

Distribution to CNS tissues was low with little, if any, radioactivity being detected in brain and spinal cord.

The distribution profile was similar between pigmented and non-pigmented animals.

Mean t1/2 was 7.5 and 9.8 h, Cmax was 1.8 and 0.716 μg equiv/mL, and AUC0-inf was 11.8 and 15.0 μg equiv•h/mL, respectively.

Tmax was 1 h after an IV dose and 4 h after a PO dose.

Cmax in most tissues was observed at 0.083 h (IV) and 4 h (PO) post-dose.

Following either an IV or PO dose, elimination was primarily in feces and bile. Approximately 91-92% of the radioactive dose was recovered after 168 h (IV) and 72 h (PO) whereas urine recovery was ≤3.1%.

CONCLUSION

SCY-078 is widely distributed after IV or PO dosing in rats. The concentrations in tissues, commonly affected by fungal infections (e.g., spleen, kidney, liver, lung and vagina), exceeded plasma concentrations by several fold. These results support development of SCY-078 for treating systemic and mucocutaneous fungal infections.