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Pharmacokinetics and Pharmacodynamics in Patients from a Phase 2, Multicenter, Open-Label, Randomized, Comparative Study of Oral SCY-078 vs. Standard-of-Care Following Initial Intravenous Echinocandin Therapy in the Treatment of Invasive Candidiasis (including Candidemia) in Hospitalized Non-neutropenic Adults

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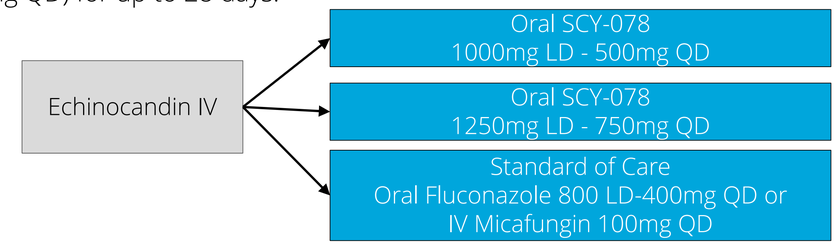
INTRODUCTION

SCY-078 is a novel intravenous and oral triterpenoid antifungal agent that is currently in clinical development for the treatment of both invasive and mucocutaneous fungal infections. It has broad-spectrum activity against both *Candida* and *Aspergillus.*

A Phase 2 study was conducted to identify the dose of SCY-078 that achieves the target $AUC_{0\text{-}24hr}$ of 15.4. μM·hr with acceptable safety and tolerability for 2 dose regimen in invasive candidiasis patient

METHODS: STUDY DESIGN

In this study, subjects with documented IC received an IV echinocandin for 3 to 10 days and were subsequently randomized to receive step-down oral therapy in a 1:1:1 ratio to one of the 3 treatment arms: oral SCY-078 1000mg loading dose followed by 500mg QD, oral SCY-078 1250mg loading dose followed by 750mg QD, or SOC (oral fluconazole 800mg loading followed by 400mg QD or IV micafungin 100mg QD) for up to 28 days.

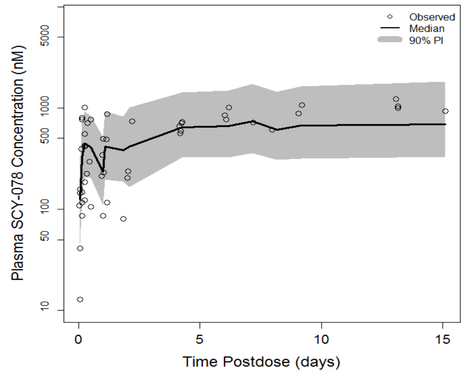


Plasma samples from SCY-078 subjects were collected to evaluate exposure by population PK modeling on day 1, day 3, day 5, day 14 and at the end of therapy (EOT) to measure $AUC_{0\text{-}24hr}$, maximum concentration (C_{max}), time to maximum concentration (T_{max}), and elimination half-life (t½). $AUC_{0\text{-}24hr}$, C_{max}, T_{max}, and t½ will be calculated by non-compartmental analysis on Day 1, followed by $AUC_{0\text{-}24hr}$ estimated by population PK analysis on each sampling day.

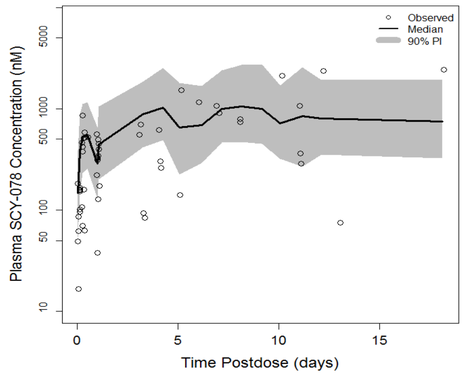
RESULTS

Mean (SD) Plasma SCY-078 Concentrations (nM) on Day 1 versus Time (Linear Scale) Pharmacokinetic Population

SCY-078 1000mg (Loading dose), 500mg (Maintenance dose)



SCY-078 1250mg (Loading dose), 750mg (Maintenance dose)



SCY-078 Global response ITT population		SCY-078 500 mg N = 6 n (%)	SCY-078 750 mg N = 7 n (%)	Fluconazole 400 mg N =7 n (%)	Micafungin 100 mg N=1 n (%)
End of Treatment	Favorable	5 (71.4)	6 (85.7)	5 (71.4)	1 (100)
	Unfavorable	2	1	2	
	Reasons for unfavorable	1. Never received study drug 2. Discontinued due to a non-drug related AE	1. Withdraw consent after one dose	1. Died (abdominal sepsis) 2. Discontinued (new + blood culture for *Candida* spp)	

The rate of adverse events (AEs) and serious AEs were similar among subjects receiving SCY-078 or fluconazole.

The most common AEs for all groups were gastrointestinal (GI); diarrhea, abdominal pain, nausea and vomiting. All GI adverse events were mild or moderate. No drug-related laboratory or ECG abnormalities. There was no related serious adverse events (SAE) to SCY-078.

Population PK analysis predicts for the SCY-078 1000mg/500mg QD and 1250mg/750mg QD dosing groups, 60 % and, 80% respectively reach the target $AUC_{0\text{-}24hr}$ of 15 μM·hr at steady state.

CONCLUSION

The result of this study indicated that an ORAL dose of 1250 mg/750 mg regimen achieved the target exposure (15 μM·hr) and was effective as step down therapy in Invasive Candidiasis in non-neutropenic adults