A Prospective, Phase 2, Multicenter, Open-Label, Randomized, Comparative Study to Estimate the Safety, Tolerability, Pharmacokinetics, and Efficacy 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 (Mycoses Study Group 010)

P. Pappas, University of Alabama at Birmingham
J. Pullman, Mercury Street Medical at Butte, MT
G. Thompson, University of California-Davis at Sacramento, CA
W. Powderly, A. Spec Washington University School of Medicine at San Louis, MO
E. Tobin, Albany Medical Center at Albany, NY
J. Vazquez, Georgia Regents University at Augusta, GA
S. Wring, D.Angulo , S. Helou Scynexis, Inc. USA
and the Investigators of the **Mycoses Study Group**

Disclosures

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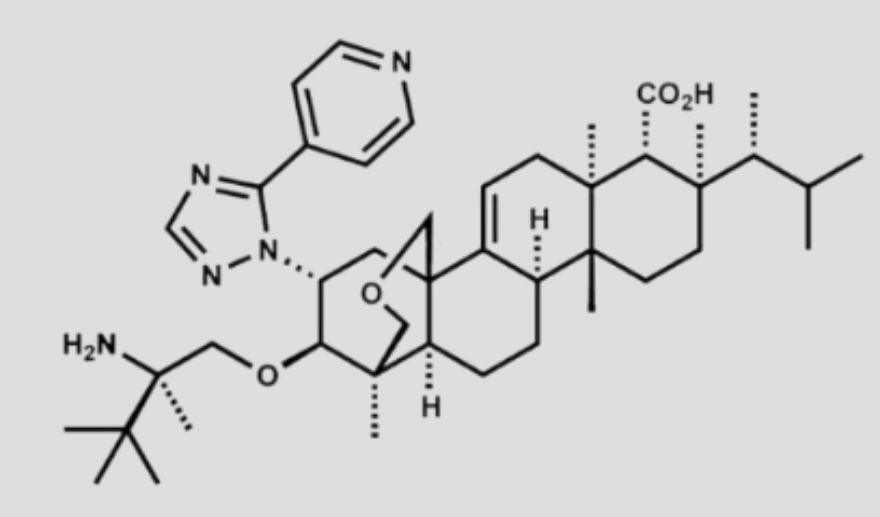
SCY-078



- An oral and intravenous semi-synthetic triterpenoid antifungal glucan synthase inhibitor, currently in development for the treatment of invasive and mucocutaneous fungal diseases
- A broad-spectrum of activity against both *Aspergillus* and *Candida* spp

SCY-078-202 Phase 2 Oral Step-Down following IV Echinocandin in IC

Objectives

- Identify an oral dose of SCY-078 that would achieve the predetermined target exposure
- Evaluate safety, tolerability and efficacy of two oral dose regiments of SCY-078 vs standard of care (Fluconazole or Micafungin IV [for fluconazole resistant organism])

Study Endpoints

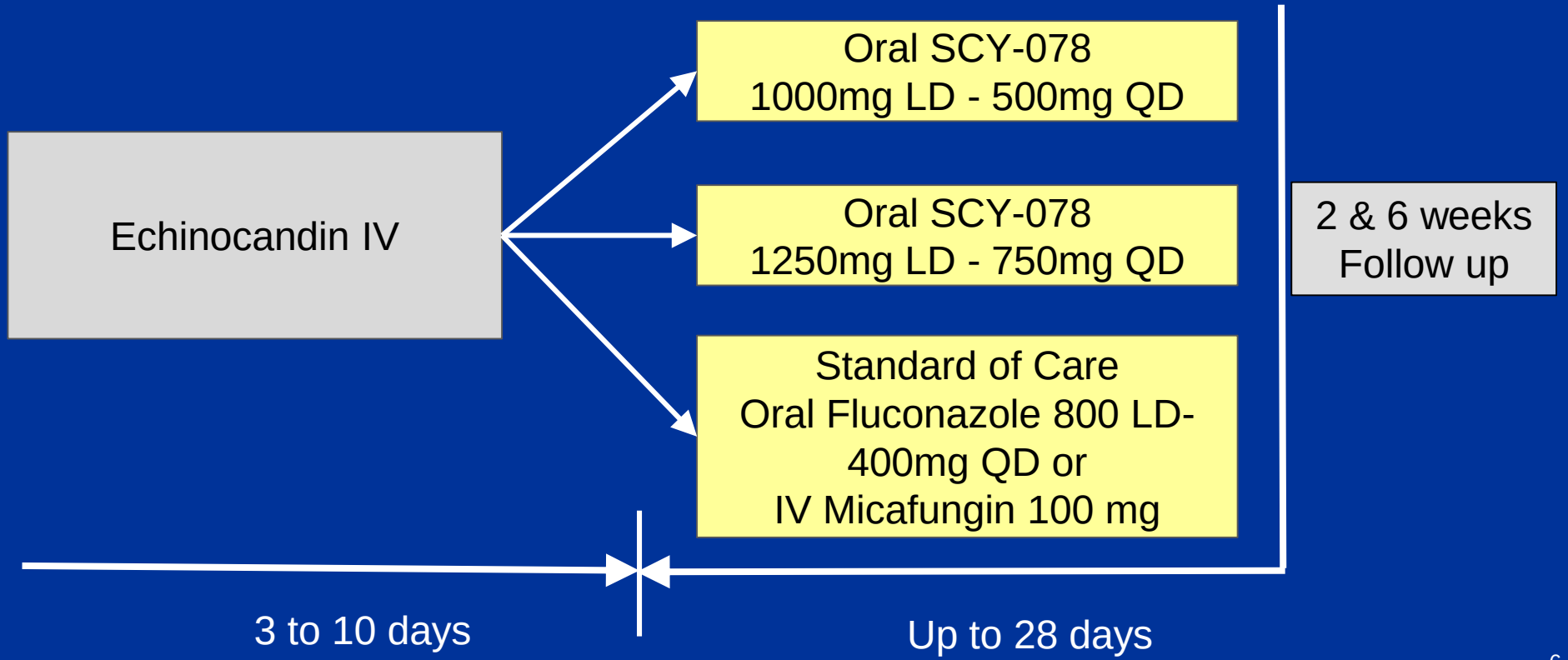
Primary Endpoint

- Safety, tolerability and PK parameters of SCY-078 administered orally

Secondary Endpoint

- Efficacy at the end of antifungal therapy assessed by global, clinical and microbiological response. Relapse was assessed at 2 and 6 weeks post treatment follow up.

Study Design



SCY-078-202 Patient Populations

Total subjects enrolled = 27
Total subjects randomized = 22

	SCY-078 500 mg n (%)	SCY-078 750 mg n (%)	Fluconazole 400 mg n (%)	Micafungin 100 mg n (%)	All Patients n (%)
Intent to Treat (ITT)	**7 (100.0)**	**7 (100.0)**	**7 (100.0)**	**1 (100.0)**	**22 (100.0)**
Per Protocol (PP)	**6 (85.7)**	**6 (85.7)**	**7 (100.0)**		**19 (100.0)**
Safety Population	**6 (85.7)**	**7 (100.0)**	**7 (100.0)**	**1 (100.0)**	**21 (100.0)**

ITT: All randomized patients

PP: Received at least 10 days of treatment and has an EOT assessment

Safety Population: All randomized who received at least 1 dose of study drug

SCY-078-202 Study Drug Exposure ITT

		SCY-078 500 mg (N=7)	SCY-078 750 mg (N=7)	Standard-of-Care Fluconazole (N=7)	Standard-of-Care Micafungin[1] (N=1)
Extent of Exposure	n	6	7	7	1
	Mean	10.7	11	13.1	2
	SD	5.13	5.45	8.36	--
Days of Randomized Study Drug	Minimum	2	1	3	2
	Median	11.5	11	13	2
	Maximum	16	19	23	2

1. Micafungin patient received 14 days of treatment but 2 of them under the protocol randomized period.

Safety Summary

- 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. One SAE related in the SOC group reported (worsening nauseas and vomiting).

Safety Summary

	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 (%)
All treatment emergent AEs (TEAEs)	6 (100)	5 (71)	7 (100)	0
Mild	4 (66.7)	1 (14.3)	3 (42.9)	-
Moderate	1 (16.7)	1 (14.3)	2 (28.6)	-
Severe	1 (16.7)	3 (42.9)	2 (28.6)	-
Drug-Related TEAEs	1 (16.7)	1 (14.3)	-	-
Mild	1 (16.7) Vomiting	1 (14.3) Diarrhea	-	-

SCY-078-202 Gastrointestinal AEs

Reported in >1 subject	SCY-078 500 mg N = 6 n (%)	SCY-078 750 mg N = 7 n (%)	Fluconazole N =7 n (%)
Gastrointestinal Disorders	3 (50.0)	3 (42.9)	3 (42.9)
Diarrhea	2 (33.3)	1 (14.3)	1 (14.3)
Abdominal Pain/Tenderness	1 (16.7)	2 (28.6)	2 (28.6) 1 (14.3)
Nausea	0	2 (28.6)	1 (14.3)
Vomiting	1 (16.7)	1 (14.3)	1 (14.3)

- All GI AEs were mild or moderate
- No drug related laboratory or ECG abnormalities
- No related SAEs

Prediction of Probability (AUC_{0-24} > 15.4 uM*hr)

Objective: Identify the dose that will result in target exposure in >80%

1000 mg (1st day), 500 mg (maintenance dose)

	Probability of AUC_{0-24} >= 15.4 uM*hr (%)	Median AUC_{0-24}	90% PI of AUC_{0-24}
Steady-state	**55.88**	**16.76**	**6.42 – 40.37**

1250 mg (1st day), 750 mg (maintenance dose)

	Probability of AUC_{0-24} >= 15.4 uM*hr (%)	Median AUC_{0-24}	90% PI of AUC_{0-24}
Steady-state	**84.46**	**27.06**	**10.42 – 64.27**

Efficacy

- The efficacy analysis was done using **Global Response Rate**
- Global Response was considered successful is there was clinical and microbiological success
  - Clinical success defined as resolution of signs and symptoms of IC
  - Microbiological success defined as the eradication of Candida spp. presented at baseline

Response Rate

- 86% (6 of 7) in the SCY-078 750mg group
- 71% (5 of 7) in the SCY-078 500mg group
- 71% (5 of 7) in the fluconazole group

SCY-078-202 Global Response ITT

		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)	
End of Follow Up	Relapse	1. New positive blood culture during the two-week FU period	0	0	

Conclusion

- 750mg/day SCY078 achieves the target exposure in ~85% of the IC population at steady state
- The oral dose of SCY-078 estimated to achieve the target exposure in subjects with IC is 750mg QD
- This dose was well-tolerated and achieved favorable global response rate similar to SOC

Dankeschön!