Evaluation of Antifungal Treatment in a Neutropenic Mouse Model of Scedosporiosis

S. ALKHAZRAJII,1 T. GEBREMARIAM,1 A. ALQARIHI,1 C. BALDIN,1 N.P. WIEDERHOLD,2 T. KITT,3 A.S. IBRAHIM,1,4

1LABiomed. Res. Inst. at Harbor-UCLA Med Ctr., Torrance, California; 2University of Texas Health Sciences at San Antonio, San Antonio, Texas; 3Astellas Pharma Global Development, Inc., Northbrook, Illinois; 4David Geffen School of Medicine at UCLA, Los Angeles, California

OBJECTIVES: Scedosporiosis is a rare fungal infection with high mortality rates. Because clinical trials are hard to conduct, we developed a murine model for evaluating the efficacy of currently used antifungals in treating scedosporiosis.

METHODS: MICs of isavuconazole (ISAV), voriconazole (VORI), posaconazole (POSA), and miconazole (MICA) were determined against 9 clinical isolates of Scedosporium apiospermum, S. boydii, and Lomentospora prolificans using the CLSI M38 method. ICR mice were intratracheally infected with S. apiospermum D16-478, a susceptible strain in all tested antifungal agents.

RESULTS: The in vitro susceptibility of MICA, ISAV, POSA, or VORI was evaluated using the Clinical and Laboratory Standards Institute (CLSI) method. MICs were determined for all four antifungal agents.

CONCLUSIONS: Despite the in vitro activity of all the tested antifungal agents against S. apiospermum, there was minimal benefit in treating neutropenic mice with any of the antifungal drugs in monotherapy. MICA at 10 mg/kg (qd) demonstrated only modest activity of any given monotherapy.


ACKNOWLEDGEMENTS: This project was funded by Astellas Pharma Global Development, Inc.