enzyme. The prodrug APX001 (APX) is in clinical development and its efficacy was evaluated in an immunocompromised murine model of disseminated C. auris.

**Methods.** MICs were determined by CLSI M27-A3 method. Mice were immuno-compromised for the study. Treatment was initiated 2 hours post challenge. IP treatment groups included a vehicle control, APX 78 mg/kg (mpk) BID; 78 mg/kg TID and 104 mg/kg BID, and sodiumaladeflun (SAD) 10mpk BID. Survival was monitored for 14 days post inoculation.

**Results.** APXA had significantly lower MIC, and MIC, values (concentration that inhibits 50 and 90% of the tested isolates, respectively) than the other tested antifungals with a MIC, of 0.031 μg/mL (Table 1).

**Conclusion.** APX was the most active antifungal agent in vitro. The prodrug APX resulted in significantly better survival than APX in a C. auris disseminated infection model. Thus APX may be a viable treatment for C. auris infections.

**Disclosures.** K. J. Shaw, Amplyx Pharmaceuticals Inc.: Employee, Salary; M. Ghanounou, Amplyx Pharmaceuticals: Consultant, Research Contractor and Scientific Advisor, Consulting fee and Research grant; Cidara Therapeutics: Consultant and Research Contractor, Consulting fee and Research grant.

**Table 1:** Susceptibility of C. auris isolates against antifungals

| Antifungal | C. auris 1 | C. auris 2 | C. auris 3 | C. auris 4 |
|------------|------------|------------|------------|------------|
| Cefiderocol | 0.015 μg/mL | 0.03 μg/mL | 0.03 μg/mL | 0.06 μg/mL |
| Ceftazidime | 0.5 μg/mL   | 1 μg/mL    | 1 μg/mL    | 2 μg/mL    |
| Meropenem   | 1 μg/mL     | 2 μg/mL    | 2 μg/mL    | 4 μg/mL    |
| Amphotericin | 0.5 μg/mL   | 1 μg/mL    | 1 μg/mL    | 2 μg/mL    |

**Friday, October 6, 2017: 12:30 PM**

**Session:** 167. Preclinical Study with New Antibiotics and Antifungals

**Background.** Azoles are the most common anti-fungal agents for the treatment of Aspergillus infections. Echinocandins have demonstrated utility in Aspergillus infections, but are limited in use due to a lack of oral bioavailability. SCY-078 is a novel, oral and intravenous (IV), tripeptidyl gluconic synthase inhibitor with activity against Aspergillus and Candida, currently in clinical development for the treatment of invasive fungal infections. This study was conducted to evaluate the in vivo antifungal activity of SCY-078 in a murine model of invasive aspergillosis (IA).

**Methods.** The in vivo activity of SCY-078 was assessed against a wild type (WT) and twoazole-resistant A. fumigatus strains in neutropenic ICR mice. Five groups of mice (6/group) were infected IV into the lateral tail vein. Antifungal therapy was initiated 2 hours post infection and maintained for 7 days. SCY-078 was administered orally as a loading dose of 15 mg/kg or 20 mg/kg followed by BID maintenance doses of 7.5 or 10 mg/kg, respectively. Caspofungin (CSF) and amphotericin B (AMB) were administered QD by intraperitoneal injection (IP) at doses of 5 mg/kg and 10 mg/kg, respectively. The primary endpoint was survival at day 14. Secondary endpoints were changes in fungal kidney burden and serum galactomannan index (GM).

**Results.** SCY-078 was well tolerated at all doses. Treatment with SCY-078 at 15 mg/kg/day and 20 mg/kg/day significantly increased mean survival in all strains (P ≤ 0.003). SCY-078 also resulted in significant reductions in fungal kidney burden (P < 0.05) and serum GM levels (P < 0.005) in all strains. Primary and secondary efficacy endpoints were met in the groups treated with IP administration of CSF or AMB. Plasma levels of SCY-078 ranged from 15–20 μM*hr (AUCmax) with Cmax ranging from 1–1.6 μg/mL for the two dose groups.

**Conclusion.** SCY-078 demonstrated potent activity against WT and azole-resistant strains of A. fumigatus in a murine model of invasive aspergillosis. The exposure needed to achieve efficacy is in line with efficacious exposures reported in the invasive candidiasis models. These results support further development of SCY-078 as an oral treatment for IA infections.

**Disclosures.** K. Borroto-Esoto, Scynexis Inc: Consultant, Consulting fee; S. Barat, Scynexis Inc: Employee, Salary; D. Angulo, Scynexis Inc: Employee, Salary; K. Holden, Evotec (UK) Ltd: Employee, Salary; P. Warn, Evotec (UK) Ltd: Employee, Salary.

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