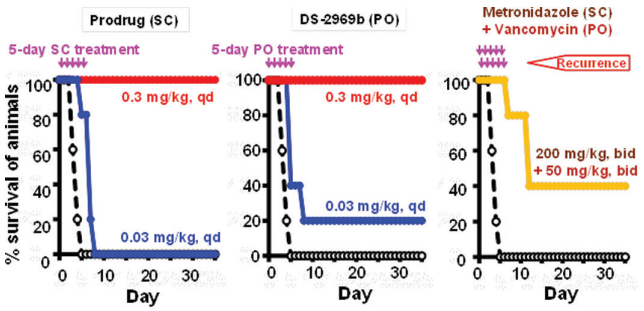

Fig. 1 Efficacy in hamster CDI model caused by *C. difficile* 2009155 (NAP1/027)

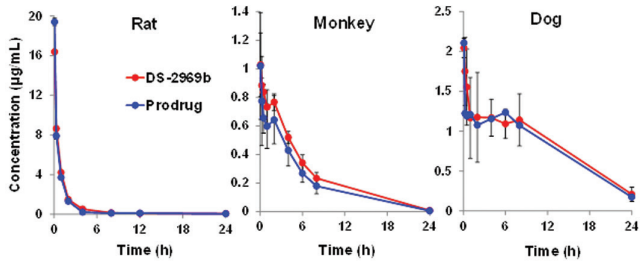

Fig. 2 Plasma concentrations of DS-2969a after IV administration of DS-2969b and its prodrug at 12.5 (rat) and 1 (monkey, dog) mg/kg as DS-2969a

Disclosures. **M. Yamada**, Daiichi Sankyo Co., Ltd.: Employee, Salary; **M. Uchiyama**, Daiichi Sankyo Co., Ltd.: Employee, Salary; **S. I. Inoue**, Daiichi Sankyo Co., Ltd.: Employee, Salary; **T. Deguchi**, Daiichi Sankyo Co., Ltd.: Employee, Salary; **Y. Furuta**, Daiichi Sankyo Co., Ltd.: Employee, Salary; **K. Yabe**, Daiichi Sankyo Co., Ltd.: Employee, Salary; **N. Masuda**, Daiichi Sankyo Co., Ltd.: Employee, Salary

1517. ZTI-01 Treatment Improves Survival of Animals Infected with Multidrug Resistant *Pseudomonas aeruginosa*

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Background. ZTI-01 (fosfomycin, FOS, for injection) is currently under US development to treat complicated urinary tract infections. ZTI-01 is unique compared with other antimicrobials in that it inhibits an early step in cell wall synthesis via covalent binding to MurA. ZTI-01 demonstrates broad *in vitro* activity against Gram-negative (GN) and -positive (GP) bacteria, including multidrug-resistant (MDR) organisms. Our study goals were to determine the efficacy of ZTI-01 as a monotherapy or in combination with meropenem against MDR *Pseudomonas aeruginosa* in a preclinical model of pulmonary infection.

Methods. 8 week old neutropenic mice were infected with a MDR strain of *P. aeruginosa* via intubation-mediated intratracheal (IMIT) instillation. 3 hours after instillation, mice received treatment with ZTI-01, meropenem, or ZTI-01 plus meropenem (combination therapy) q8h for 5 days. Mice were monitored every 8 hours for 7 days for development of disease and moribund animals were humanely euthanized. Lungs and spleens were harvested at euthanasia, or at 7 days for survivors, and processed for bacterial enumeration and development of pathology.

Results. Mice were challenged with a lethal dose of *P. aeruginosa* UNC-D. Mock treated animals succumbed to infection within 36 hours post-infection. Animals that received 6 g/kg/day ZTI-01 showed an increase in the MTD (52 hours) and 25% of the cohort were protected from lethal disease. Combining ZTI-01 with meropenem resulted in a significant increase in survival (≥75% of cohorts survived infection). Combination therapy also significantly decreased bacterial numbers in the lungs and inhibited dissemination to the spleens. Furthermore, animals receiving combination therapy were protected from significant inflammation in the lungs and the development of pneumonia.

Conclusion. Here we report that combination therapy with ZTI-01 and meropenem provides significant improvements in all disease manifestations over treatment with each drug individually in a preclinical model for pulmonary infection with MDR *P. aeruginosa*. These data strongly support further evaluation of ZTI-01 in combination with other antibiotics as potential therapies against pulmonary infections with MDR bacteria.

Disclosures. **E. J. Ellis-Grosse**, Zavante Therapeutics, Inc.: Employee and Shareholder, Salary

1518. Evaluation of the Efficacy of CD101, a Novel Echinocandin, in the Treatment of *Candida auris* Infection Using a Murine Model of Disseminated Candidiasis

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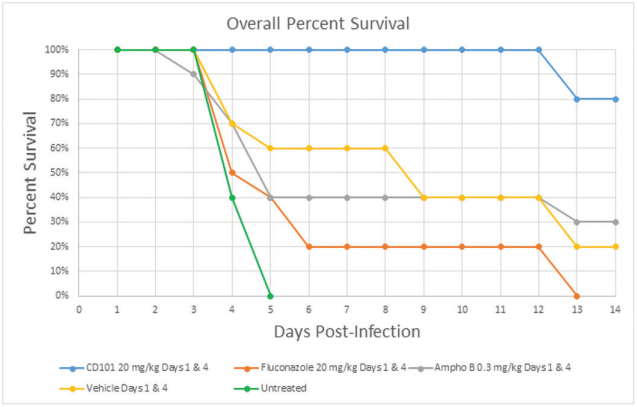
Background. The first case of an invasive infection caused by *C. auris* was reported in July of 2016. Multiple cases have since been reported with high mortality rates due to the multidrug-resistant nature of *C. auris*. Although *C. auris* shows increased susceptibility to the echinocandin class of antifungals, the use of these drugs is restricted to multiple IV administrations. CD101 is a novel echinocandin with enhanced stability and pharmacokinetics, allowing for once weekly high dose administration. In this study, we evaluated the efficacy of CD101 in the treatment of disseminated *C. auris* infection using a murine model of disseminated candidiasis.

Methods. Female 6–8 week old CD-1 mice were immunosuppressed with cyclophosphamide (200 mg/kg) 3 days prior to infection and 150 mg/kg 1 day post-infection. On the day of infection, mice were inoculated with 3 x 10^7 *C. auris* blastospores via the lateral tail vein. Mice were randomized into 5 groups ($n = 5$ for colony forming units (CFU) and $n = 10$ for survival): CD101 20 mg/kg administered by intraperitoneal (IP) injection, fluconazole 20 mg/kg administered per os (PO), amphotericin B 0.3 mg/kg IP, and a vehicle control. Treatments were administered 2 hours post-infection (day 1) and again on day 4 of the study for a total of 2 doses. Mice were monitored daily and a survival curve was generated. CFU groups were sacrificed on day 8 of the study. One kidney was removed from each mouse, homogenized, plated on potato dextrose agar (PDA), and incubated at 35°C for 2 days to determine CFU. The remaining survival mice were monitored until the end of the study (day 14).

Results. CD101 showed an average 3 log reduction in kidney CFU compared with fluconazole, amphotericin B, and vehicle treated groups, which was statistically significant ($P = 0.03$, 0.03, and 0.04, respectively). At the end of the study, percent survival of mice in CD101, fluconazole, amphotericin B, vehicle, and untreated groups was 80, 0, 30, 20, and 0%, respectively (Figure 1).

Conclusion. Taken together, our findings show that CD101 possesses potent antifungal activity against *C. auris* infection in a disseminated model of candidiasis. Additionally, treatment with CD101 resulted in a significantly higher overall percent survival. Further investigation of this drug is warranted.

Figure 1. Survival curve of mice in all treatment groups after 14 days.



Disclosures. **M. Ghannoum**, Amplyx Pharmaceuticals: Consultant, Research Contractor and Scientific Advisor, Consulting fee and Research grant; Cidara Therapeutics: Consultant and Research Contractor, Consulting fee and Research grant

1519. Delayed Therapy with Plasma Gelsolin Improves Survival in Murine Pneumococcal Pneumonia

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Background. Innate immune responses contribute to successful resolution of bacterial pneumonia. Bolstering host defense with immunomodulators might be increasingly needed to improve outcomes in antibiotic-resistant infections. One