

Evaluation of the efficacy of rezafungin in the treatment of *Candida albicans* endophthalmitis using a rabbit model

Lisa Long¹, Janet Herrada¹, Daniel Caley¹, Gustavo Munguba¹, Rania Sherif¹, Ken Bartizal², Mahmoud A. Ghannoum^{*1,3}

¹Case Western Reserve University, University Hospitals Cleveland Medical, Cleveland, United States, ²Cidara Therapeutics Inc., San Diego, United States, ³NTS Ventures, Cleveland, United States

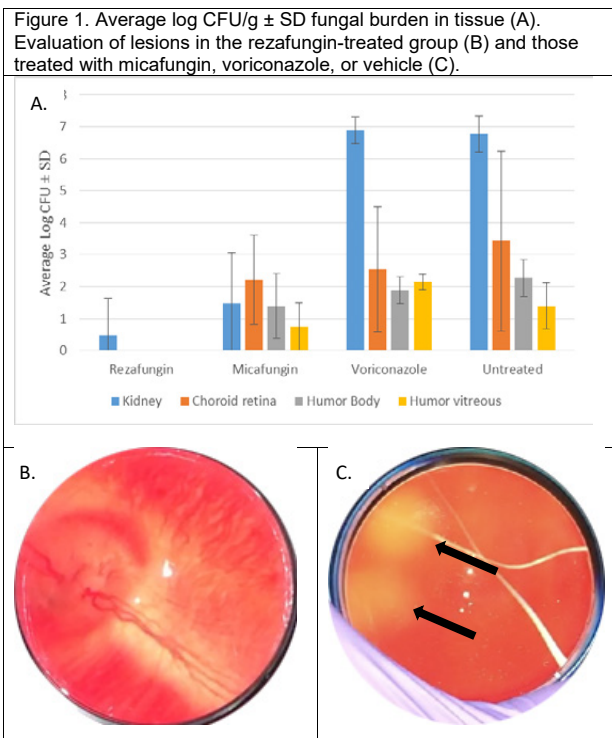
Abstract third-party references: Cidara Therapeutics Inc.

Background: *Candida* endophthalmitis is a devastating disease. Echinocandins are first-line therapy for candidemia and invasive candidiasis, however, due to poor penetration of currently approved echinocandins into the eye, once *Candida* eye involvement is demonstrated, current guidelines recommend a switch to azole therapy. The aim of this study was to evaluate the efficacy of rezafungin, a novel echinocandin with unique PK properties, in the treatment of endophthalmitis in a rabbit candidiasis model.

Materials/methods: New Zealand White rabbits with indwelling catheters were inoculated intravenously with 5×10^6 colony-forming units (CFU) of *Candida albicans* SC5314 and divided into groups: rezafungin 10mg/kg (n=6), micafungin 6.2mg/kg (n=5), voriconazole 10mg/kg (n=4) and vehicle control (n=5). Treatments were administered IV at 0 and 80h post-inoculation. Day 8, the rabbits were anesthetized and indirect ophthalmoscopy performed. Tissues were collected for assessment of fungal burden. Eye scores were given based on the number and size of lesions and total ocular damage caused by infection. The severity of each lesion was scored on a 1-4 scale: 1+, lesion barely visible; 2+, lesion small but easily visible; 3+, lesion large but less than one disk diameter in size; and 4+, lesion larger than one disk diameter.

Results: In the kidneys, the voriconazole and vehicle groups had the highest CFU counts, while the rezafungin group showed the lowest (Fig. 1A). The rezafungin- and micafungin-treated groups showed significantly lower bioburden when compared to the voriconazole and vehicle groups ($P < 0.001$). In the retina, humor body, and vitreous humor, the greatest bioburden was observed in vehicle control-treated animals as expected. Animals treated with rezafungin demonstrated no detectable CFU. The rezafungin-treated group compared with the micafungin, voriconazole and vehicle groups showed significantly fewer CFU in the retina ($P < 0.05$), humor body ($P < 0.001$), and vitreous humor ($P < 0.05$). Eye Score— The rezafungin-treated group demonstrated no eye lesions (Fig.1B), while the micafungin, voriconazole and vehicle (Fig.1C) groups showed average eye scores of 1.9, 2.5, and 3.2, respectively.

Conclusions: Our findings show that rezafungin is effective in the treatment of endophthalmitis caused by *C. albicans*.



Presenter email address: mahmoud.ghannoum@case.edu