CD101 Gel Formulation is Highly Efficacious Against Azole-Resistant Candida albicans in a Rat Model of Vulvovaginal Candidiasis

V. Ong¹, K. Bartizal¹, D. Hughes¹, L. Miesel²
¹Cidarata Therapeutics, San Diego, CA, ²Eurofins Panlabs, Taipei, Taiwan

RESULTS

In earlier rat VVC studies, topical CD101 gel given BID eradicated azole-susceptible C. albicans (ATCC 44858) up to at least 1 week after treatment cessation². Fluconazole given orally showed modest improvement whereas topical miconazole (2% cream) showed fungal rebound less than 1 week after treatment cessation.

RESULTS (cont’d)

With optimization, a slower release gel formulation of CD101 was developed that enabled once daily (QD) topical administration. This slower release CD101 gel formulation was found to be highly effective in the rat VVC model of azole-resistant C. albicans (R357). The vaginal lavage CFU showed that topical CD101 cleared the vaginal infection and reduced fungal burden for at least 1 week after treatment cessation. Nystatin (2.3% or 100,000 USP/g), a polyene antifungal, did not appear to reduce vaginal CFU as effectively as on day 5 compared to CD101.

CONCLUSIONS

CD101 is a novel stable and long-acting echinocandin, demonstrated efficacy in mouse disseminated infection as well as rat VVC models of azole-resistant candidiasis. The CFU reduction in these tested models shows that CD101 is fungicidal in vivo against C. albicans.

REFERENCES

   1. Miesel, et al., ASM Microbe 2016, Efficacy of a Novel Echinocandin, CD101, in a Mouse Model of Candida albicans disseminated infection (R357). We have subsequently developed mouse disseminated and rat VVC infection models using an azole-resistant C. albicans strain (R357). The results of these studies are presented and discussed in this position.

INTRODUCTION

CD101 is a novel echinocandin being developed for the treatment of fungal infections. Echinocandins have been successfully and safely used as intravenous antifungal therapy for 15 years. Like previously approved echinocandins, CD101 is fungicidal against Candida spp. Unlike previously approved echinocandins, CD101 has a uniquely stabilized structure enabling it to be formulated for topical administration and developed for treatment of VVC.

CD101 is a novel echinocandin being developed for the treatment of fungal infections. Echinocandins have been successfully and safely used as intravenous antifungal therapy for 15 years. Like previously approved echinocandins, CD101 is fungicidal against Candida spp. Unlike previously approved echinocandins, CD101 has a uniquely stabilized structure enabling it to be formulated for topical administration and developed for treatment of VVC.

CD101 was designed to be a highly stable molecule and has shown robust efficacy in mouse infection models of disseminated Candida/Aspergillus. CD101 has an excellent nonclinical safety and toxicology profile enabling high concentration, front-loaded doses, and is currently in Phase 2 clinical trials for candidemia and vulvovaginal candidiasis (VVC).

Topical formulations of CD101 were optimized and found to be efficacious using a rat VVC model. Initial rat VVC studies were performed using an azole-susceptible C. albicans strain (ATCC 44858). We have subsequently developed mouse disseminated and rat VVC infection models using an azole-resistant C. albicans strain (R357). The results of these studies are presented and discussed in this position.

METHODS

Mouse disseminated infection model
• Neutrophil ICR Mice (n = 5/group)
• Cyclophosphamide on Days -4 (150 mg/kg) and -1 (100 mg/kg)
• Infection – Day 0, 5 x 10⁵ CFU/mouse
• Vehicle or CD101 – Intraperitoneal (IP)

Rat VVC model
• Oophorohysterectomized Wistar Rats (n = 5/group)
• 17β-estradiol (10 mg/kg) 3 days before infection and 4 mg/kg/week
• Dexamethasone (2 mg/kg) added to drinking water
• Vaginal infection – Day 0. C. albicans (ATCC 44858 or R357)
• 10⁵ CFU/inocula
• Treatment starts 2 days after infection for 3 days, Days 2 to 4
• Vaginal lavage: CU from separate groups Day 5 to 12 after infection (1 to 8 days after treatment cessation)

Vaginal infection
• Vaginal lavage CFU on days 5 to 12 after infection

RESULTS

CD101 was designed to be a highly stable molecule and has shown robust efficacy in mouse infection models of disseminated Candida/Aspergillus. CD101 has an excellent nonclinical safety and toxicology profile enabling high concentration, front-loaded doses, and is currently in Phase 2 clinical trials for candidemia and vulvovaginal candidiasis (VVC).

Topical formulations of CD101 were optimized and found to be efficacious using a rat VVC model. Initial rat VVC studies were performed using an azole-susceptible C. albicans strain (ATCC 44858). We have subsequently developed mouse disseminated and rat VVC infection models using an azole-resistant C. albicans strain (R357). The results of these studies are presented and discussed in this position.