Novel Echinocandin CD101 Gel Formulation is Highly Effective in Eradicating Candida albicans in a Rat Model of Vulvovaginal Candidiasis

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Abstract
Background: Efficacy of vaginal administration of CD101, a novel long-acting and highly stable echinocandin, formulated as a gel compared to marketed 2% miconazole cream in an immunosuppressed rat model of vulvovaginal candidiasis (VVC). Currently marketed echinocandins lack chemical stability to be effectively formulated for topical administration.

Methods: Groups of five oophorohysterectomized female rats were used. Estradiol (200 µg) was administered at 10 mg/kg subcutaneously 3 days before C. albicans (ATCC 44858) challenge then maintained with 4 mg/kg weekly injections throughout the study. Animals were immunosuppressed with dexamethasone applied in drinking water (2 mg/L) 3 days before challenge and throughout the study. To establish vaginal infection, oophorohysterectomized rats were inoculated intravaginally with C. albicans (10⁹ CFU) in PBS. All treatments began 48 hours after challenge. CD101 gels, 3%, and 10% and miconazole 2%, were administered intravaginally at 0.1 mL/rat twice daily for 5 days. Rats were sacrificed at time points (1, 3, 5, and 8 days) after infection, and vaginal lavage was performed and the fungal counts in the vaginal fluid were measured in lavage fluid. Unpaired Student’s t test was performed to determine the significance of treatment effects relative to the vehicle control group.

Results: All test articles resulted in significant reductions in fungal counts relative to the vehicle controls (* p < 0.05). However, results suggested that CD101, appears more effective than miconazole, and the 3% formulation was more effective than the 10% and 2% miconazole formulations. The 2% miconazole was not effective at these time points. CD101 showed prolonged efficacy after qd dosing (C) Slower-release cream/ointment formulations of CD101 showed prolonged efficacy after qd dosing. Miconazole cream bid (MCZ, Mycoderin) was the second most effective at eliminating detectable fungal counts (≤LOD). CD101 3% topically applied significantly reduced fungal counts 1 week after treatment cessation.

Conclusions: CD101 gel and cream/ointment formulations, and positive controls agents miconazole (Mycoderm Pharmacy topical cream formulation), and oral fluconazole were used. Treatment Antifungal therapy was started 48 hours after infection (D2). Groups of 5 rats each were treated intravaginally with vehicle and test articles, once (qd) or twice daily (bid) for 3 consecutive days. Rats were euthanized and CO2 asphyxiation at time points 12 hr after the last dose (D5 to D12 after infection). Vaginal fungal burden was evaluated in one animal from each group, one day after infection (24 hr before treatment start). Test articles Topical CD101 gel and cream/ointment formulations, and positive controls agents miconazole (Mycoderm Pharmacy topical cream formulation), and oral fluconazole were used.

CD101 3% Topical Gel bid

Conflicts of Interest

Acknowledgment
We thank A. Amegah and J. Locke for the CD101 time-kill data, and Latitude Pharmaceuticals for formulation development efforts. This study was funded by a research grant from Cidara Therapeutics, Inc.

Reference