Prophylactic, single-dose, subcutaneous (SC) administration of CD101 shows robust efficacy in neutropenic mouse models of candidiasis and aspergillosis

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Background: Fungal infections pose a significant public health burden with high morbidity and mortality. Immunocompromised patients continue to be at risk for opportunistic infections caused by fungal pathogens, such as Candida spp. and Aspergillus spp. CD101 is a novel echinocandin that has demonstrated robust preclinical efficacy and is differentiated from currently available echinocandins by a long-acting pharmacokinetic profile, allowing for once-weekly intravenous dosing, and exceptional stability and solubility, enabling formulations for topical and subcutaneous (SC) administration. The potential for intermittent SC administration may extend the utility of CD101 beyond that of other echinocandins, to include antifungal treatment and prophylaxis in the outpatient setting. Neutropenic mouse models of candidiasis and aspergillosis were used to evaluate the in vivo efficacy of single SC doses of CD101 as antifungal prophylaxis.

Material/methods: Candidiasis model: ICR mice (5/grp) were rendered neutropenic by cyclophosphamide on day -4 (150 mg/kg) and day -1 (100 mg/kg), then challenged (day 0) with Candida albicans ATCC SC5314 via IV (100 µL, 10⁵ CFU/mouse). Prior to challenge, mice were given one SC dose (5, 10, or 20 mg/kg) of CD101 on day -5, -3, or -1. At 24 hours postchallenge, kidneys were removed for CFU enumeration.

Aspergillosis model: ICR mice (6/grp) were rendered neutropenic by cyclophosphamide on days -3 (6 mg/mouse), +1 and +4 (2 mg/mouse). Challenge with Aspergillus fumigatus ATCC 13073 via IV (100 µL, 10⁴ CFU/mouse) occurred on day 0. Prior to challenge, mice were given one SC dose (5, 10 or 20 mg/kg) of CD101 on day -5, -3, or -1. Survival was monitored for 14 days.

Results: In the candidiasis model (Figure 1a), kidney CFU decreased with increasing doses of CD101 and prophylaxis occurring closer to challenge. Complete clearance was observed in all animals.
receiving 10 mg/kg at days -3 and -1 and all but one animal receiving 20 mg/kg on day -3. At doses of 5 or 10 mg/kg, prophylaxis with CD101 demonstrated a significant decrease in CFU at day -3 and -1. At the highest dose of 20 mg/kg, CD101 reduced CFU burden regardless of prophylactic treatment day.

In the aspergillosis model (Figure 1b), survival was monitored for 14 days after challenge. Subcutaneous CD101 at 5, 10, and 20 mg/kg on day -5, -3 or -1 were associated with significant (>50%) increases in survival compared with vehicle. The 5 mg/kg group showed increased survival when prophylaxis was given closer to challenge. All animals in the 10 and 20 mg/kg groups survived regardless of prophylactic treatment day.

**Conclusions:** CD101, a novel echinocandin, administered in a single SC dose was found to be protective against fungal challenge. CD101 SC may provide a potential new agent and route of administration for intermittent outpatient echinocandin treatment and prophylaxis.

![Figure 1a. CD101 prophylaxis in mouse candidiasis: kidney fungal burden in controls (vehicle, at 2 and 24 hrs post-challenge) and by dose and time of CD101 prophylaxis (at 24 hrs post-challenge)](image1a)

![Figure 1b. CD101 prophylaxis in mouse aspergillosis: 14-day survival rates in vehicle and CD101 prophylaxis group](image1b)