**Efficacy of cochleated amphotericin B (C-AMB) in mouse models of oropharyngeal and vulvovaginal candidiasis**

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**Abstract**

**Introduction:** *Candida albicans* causes debilitating mucosal infections in patients with inherited susceptibility to chronic mucocutaneous candidiasis (CMC) such as oropharyngeal candidiasis (OPC) and vulvovaginal candidiasis (VVC), which often require long-term azole-based treatment. Due to the high incidence of azole resistance in these patients, alternative treatment options are desirable. Acquired resistance against amphotericin B (AMB) has not been documented but parenteral administration of AMB is associated with nephrotoxicity and infusion reactions.

**Cochleated AMB (C-AMB)** is a new formulation of AMB designed for oral administration and thus an attractive treatment option for OPC and VVC. The purpose of our study was to assess the efficacy of C-AMB in mouse models OPC and VVC.

**Methods:** IL-17 signaling deficient mice (Act1−/−) were infected with a clinical isolate of *C. albicans* in models of OPC and VVC. From day 1 post-infection (pi) through day 4 pi, mice were treated once daily via oral gavage with C-AMB or placebo or intraperitoneal AMB-deoxycholate (AMB-d). At day 5 pi, the mice were euthanized and tongue tissue (OPC) or vaginal tissue and vaginal tissue (VVC) were harvested to quantify fungal burden.

**Results:** During OPC, mice treated with C-AMB (25 or 83.5 mg/kg/day) displayed significantly reduced tongue fungal burden compared to placebo-treated mice and comparable to that observed in mice treated with intraperitoneal AMB-d (25 mg/kg/day). During VVC, mice treated with C-AMB exhibited significantly decreased fungal burden in vaginal tissue, but not vaginal fluid, relative to placebo-treated mice.

**Conclusions:** Oral administration of C-AMB in IL-17-signaling deficient mice results in a reduction in tongue and vaginal tissue fungal burden during mucosal *C. albicans* infections. Ongoing studies are aimed at characterizing the distribution of C-AMB in mouse mucosal tissues and examining C-AMB efficacy relative to fluconazole.

**Background and Rationale**

**Candida albicans and the host**

- High disease burden for mucosal candidiasis
  - Oropharyngeal candidiasis: ~2 million cases/year globally
  - Vulvovaginal candidiasis: ~138 million cases/year globally
- High cost for disease management
- High incidence of resistance with standard of care antifungals

**Rationale**

- **High disease burden for mucosal candidiasis**
  - Oropharyngeal candidiasis: ~2 million cases/year globally
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- **High cost for disease management**
- **High incidence of resistance with standard of care antifungals**

**Results**

Oral administration of **cochleated amphotericin B** (C-AMB) effectively reduces tongue fungal burden during OPC in mice.

**Summary**

- Oral administration of C-AMB in IL-17-signaling deficient mice results in a reduction in tongue tissue fungal burden during OPC.
- Orally administered C-AMB shows comparable efficacy to intraperitoneal AMB-d.
- Oral administration of C-AMB is efficacious at reducing vaginal tissue fungal burden during VVC in mice.

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