Optimization of CD101 Formulation Against *Candida albicans* in a Rat Model of Vulvovaginal Candidiasis

Voon Ong, PhD
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**Background**

- Vulvovaginal candidiasis (VVC) is a highly prevalent *mucosal* infection
- VVC is caused by *Candida albicans* (~85%) and *non-albicans* (~15%)
- 5-8% of women have *recurrent VVC* (RVVC) which is associated with a negative impact on work/social life
- *Oral fluconazole* prescribed despite relapse, potential DDIs and increased risk to pregnant women
- No FDA-approved therapy for RVVC and *no novel agent in >20 years*
CD101 - A novel echinocandin antifungal

- Echinocandins have potent **fungicidal** activity against *Candida* species
- However, current echinocandins have limited stability making them unsuitable for topical formulation/application
- CD101 is a novel echinocandin with **remarkable chemical/biological stability**

\[ \text{C. albicans (n=351)} \]
\[ \text{MIC}_{90} = 0.06 \mu g/mL \]

\[ \text{C. glabrata (n=200)} \]
\[ \text{MIC}_{90} = 0.06 \mu g/mL \]
Rat VVC model*

- Oophorectomized rat - preconditioned with estradiol and dexamethasone
- Challenge - *C. albicans* (ATCC 44858), $10^7$ CFU/rat

Can CD101 improve outcome vs current therapies?

Opportunity

MIC
Fluconazole = 0.25 µg/mL
Miconazole = 0.06 µg/mL
CD101 = 0.25 µg/mL

Flu PO
20 mg/kg
QD

2%Miconazole
(Gyno-Mycoderin)
BID
Can CD101 improve outcome vs current therapies? Yes
Drug Release

- Marketed products show a wide range of % release
  - Miconazole cream used daily for 7 days (>60% in 24 h)
  - Tioconazole ointment used as single application (9% in 24 h)
  - Butoconazole SR used as single application (2% in 24 h)

- Initial CD101 gel formulation releases >60% in 24 h

- Quick math check: 1% release from a 3% (w/w) drug containing formulation = 300 µg per gram applied
QD: Fast Release vs Slow Release

% Drug Release in 24 h

>60% 9%

Miconazole less effective QD
QD: Fast Release vs Slow Release

% Drug Release in 24 h

>60%  9%   90%   70%   1%

Log CFU/rat lavage

LOD: 0.7
QD: Moderate Release vs Slow Release

% Drug Release in 24 h

16% 6% 1%

log CFU/rat lavage

LOD 0.7
QD: Optimized Formulation

Log CFU/rat lavage

LOD 0.7

No treatment

Fluconazole PO 20 mg/kg QD

2% Miconazole Cream BID

3% CD 101 Ointment QD
Conclusions

- CD101 gel and cream/ointment formulations are highly effective at reducing *C. albicans* burden in the rat VVC model.
- 3% CD101 as a slow release ointment QD significantly reduced the fungal burden for up to 1 week after treatment cessation.
- 3% CD101 slow release ointment comparable or better than topical 2% miconazole or oral fluconazole.
- Topical CD101 is a promising alternative for the treatment of VVC (currently in Ph2 clinical testing).