



# Efficacy of a Novel Echinocandin, CD101, in a Mouse Model of Azole-Resistant Disseminated Candidiasis

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- **Lynn Miesel is a Eurofins Pharma Discovery Services employee.**
- **This research was performed under contract between Eurofins Panlabs Taiwan and Cidara Therapeutics.**

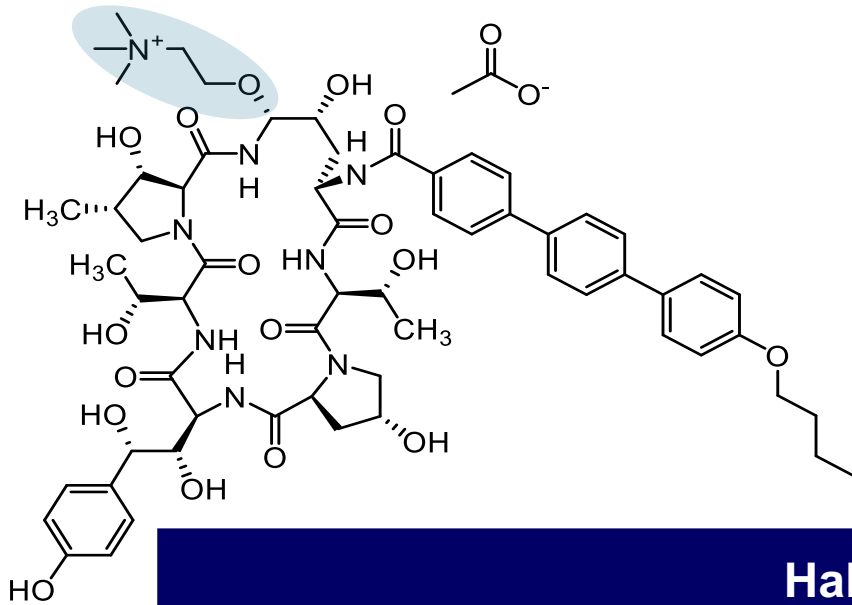
- **Candidiasis is becoming more prevalent among nosocomial infections, ranking fourth among BSIs in the USA (1)**
- ***C. albicans* is the predominant cause but non-*albicans* species are increasingly prevalent**
- **Resistance to azole antifungals is now more common due to widespread fluconazole use**
- **The IDSA and ESCMID now recommend echinocandins as first-line treatment (2, 3)**
- **This study aimed to test CD101 for potential use against azole-resistant candidiasis using a disseminated mouse infection model**

(1) M. Sanguinetti, B. Posteraro, and C. Lass-Flörl. 2015 *Mycoses*. 58 p2-13

(2) PG Pappas et al. 2015 *Clinical Infectious Disease*

(3) OA Cornely et al. 2012 *Clin Microbiol Infect*. 18 Suppl 7 p19–37

# CD101, a highly stable echinocandin



- Enhanced chemical stability
- Long-acting pharmacokinetics
- In development for once-weekly therapy

Half-life (hr)			
Species	Caspofungin <sup>a</sup>	Anidulafungin <sup>b</sup>	CD101 <sup>b</sup>
SD Rat	6-7	22	30
Dog	N/A	12	53
Cyno Monkey	N/A	8	40
Chimpanzee	5-8	30	81

<sup>a</sup> R. Hajdu, et al. *Antimicrob. Agents Chemother.* (1997) 41:2339–2344

<sup>b</sup> K. James, et al. *ICAAC* (2014) A-693 and A-694

## *Candida albicans* 2012 – 2014 clinical isolates (n=100)\*

	Azole-susceptible (n=90)	Fluconazole-resistant (n=10)
MIC <sub>90</sub> (µg/mL)	0.03	0.03

- **CD101 has potent in vitro activity against azole-susceptible and -resistant clinical isolates**

\*D Hall, R Bonifas, DL Shinabarger, and CM Pillar. Evaluation of the In Vitro Activity of CD101, a Novel Echinocandin, and Comparators Against Recent Clinical Isolates of *Candida* spp. *ICAAC/ICC* (2015) M-850

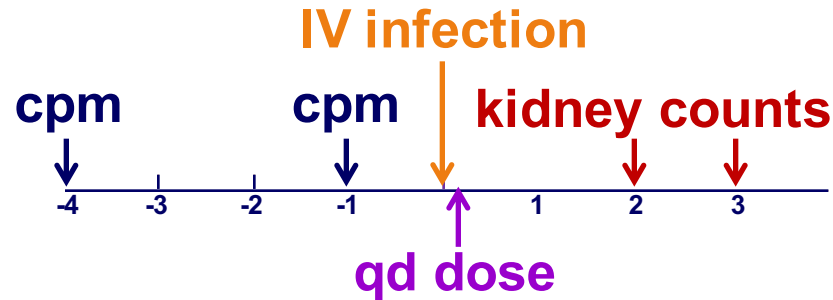
***C. albicans* strain R357 is an azole-resistant human blood isolate**

Antifungal agent	Endpoint (% inhibition)	MIC ( $\mu\text{g/mL}$ )	Susceptibility (CLSI)
Fluconazole	50%	>64	R
Voriconazole	50%	>64	R
Posaconazole	50%	>64	
Amphotericin B	100%	0.5	S
Caspofungin	50%	0.25	S
CD101	50%	0.125	

## Azole resistance in R357

- CaERG11 increased expression: 12.3x
- CaERG11 changes: D116E, D153E, and E266D
- No significant changes in CDR1 or MDR1 expression

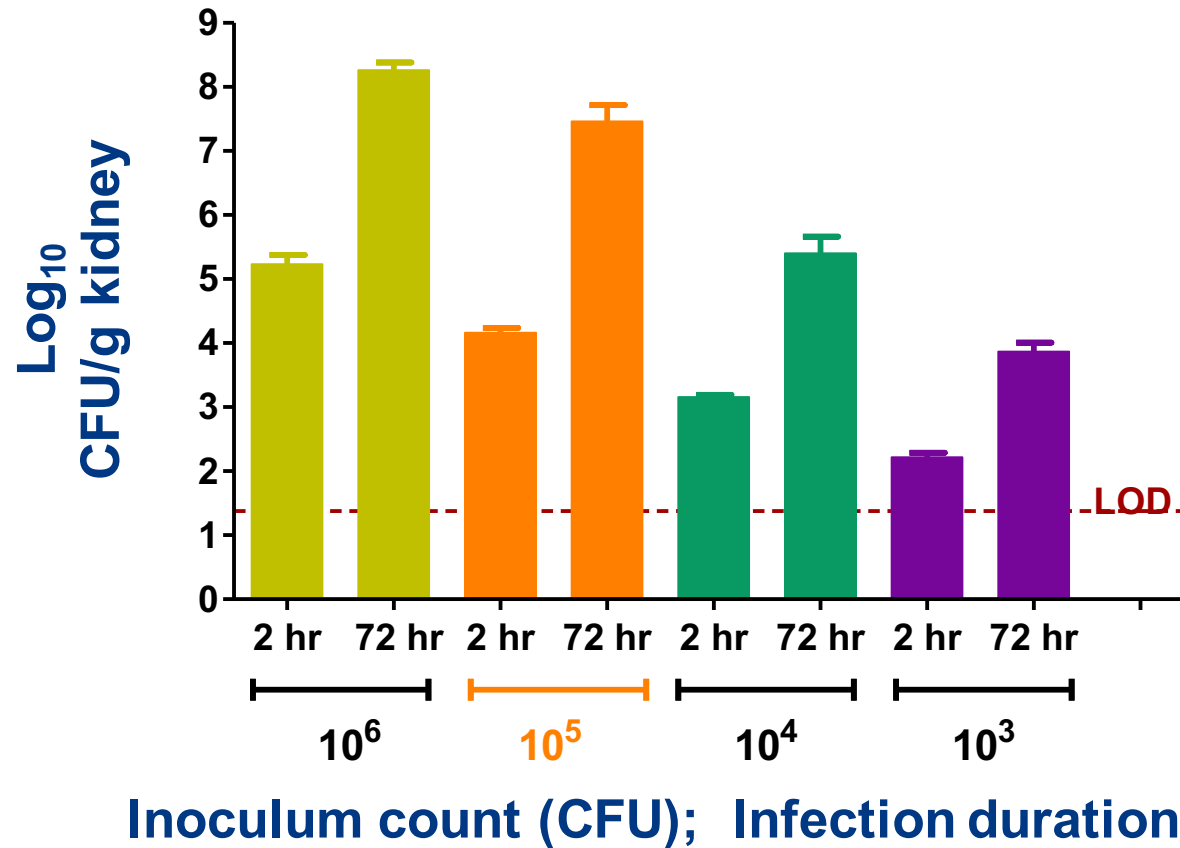
# Azole-resistant *C. albicans* R357 disseminated infection model



## Procedure

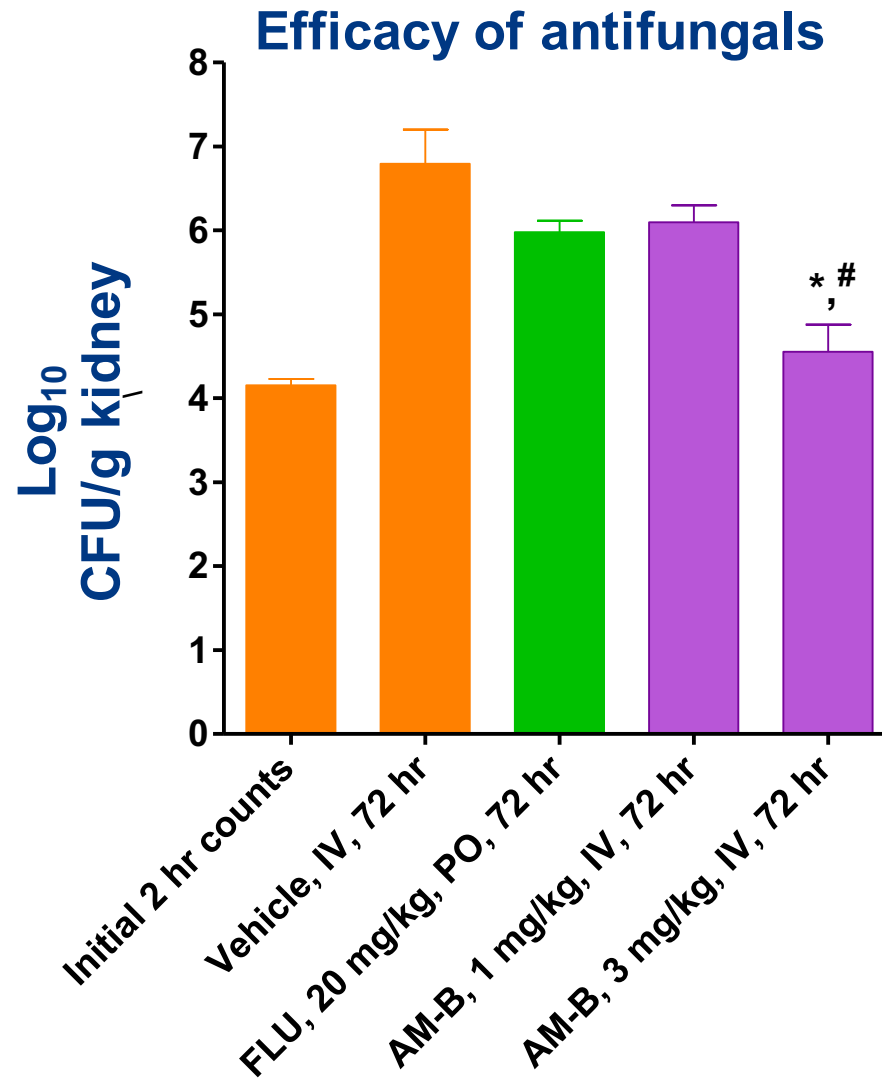
- Host: ICR Mouse
- Neutropenia – cyclophosphamide (cpm) days -4, -1
- Infection, *Candida albicans* R357,  $10^5$  CFU/mouse
- Test article administration: one (qd) dose
  - 2 hr after infection
  - Vehicle, CD101 – Intraperitoneal (IP)
  - Amphotericin B (AM-B) – Intravenous (IV)
  - Fluconazole (FLU) – oral (PO)
- Kidney counts (CFU /g) – 48, 72 hr after infection

## Model development – vary the inoculum density



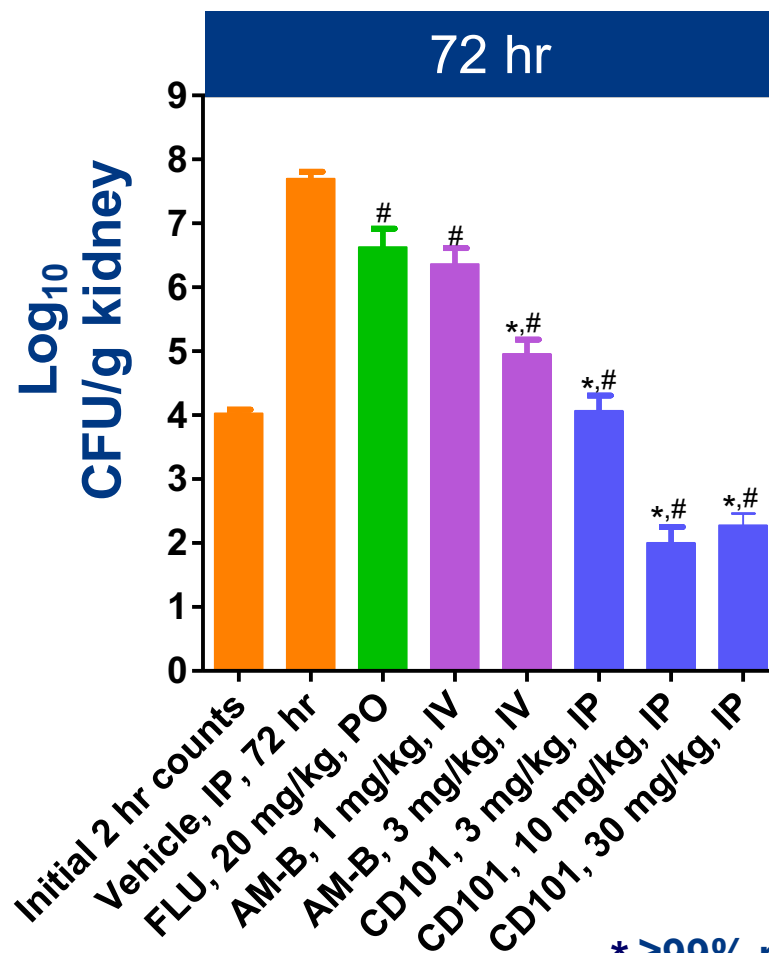
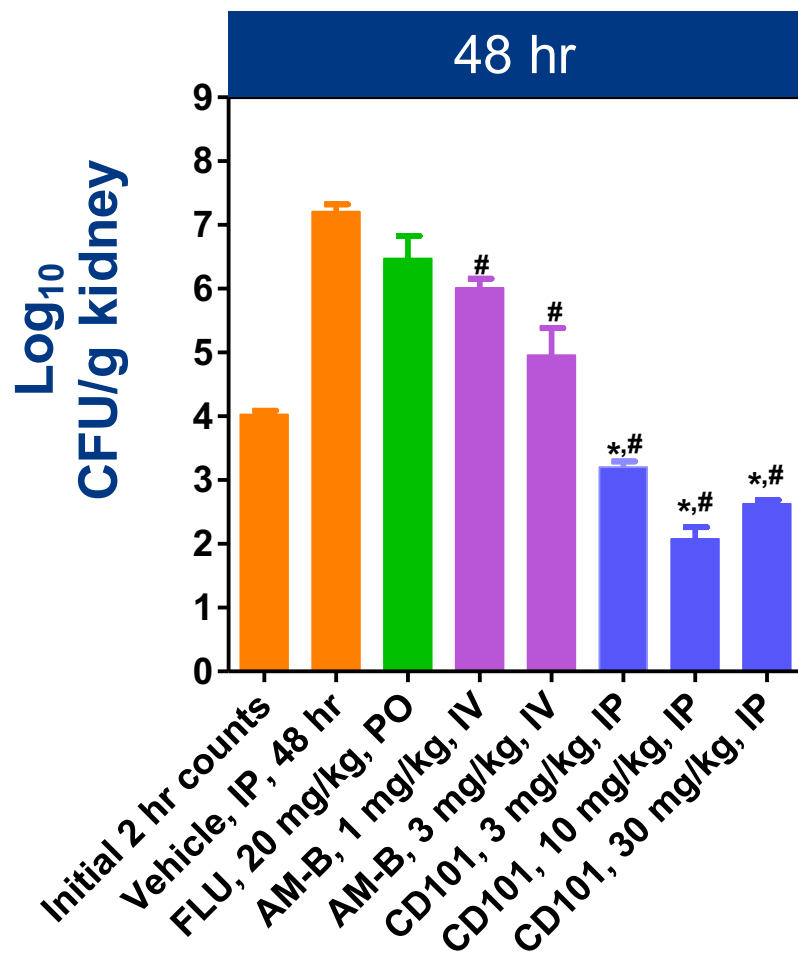


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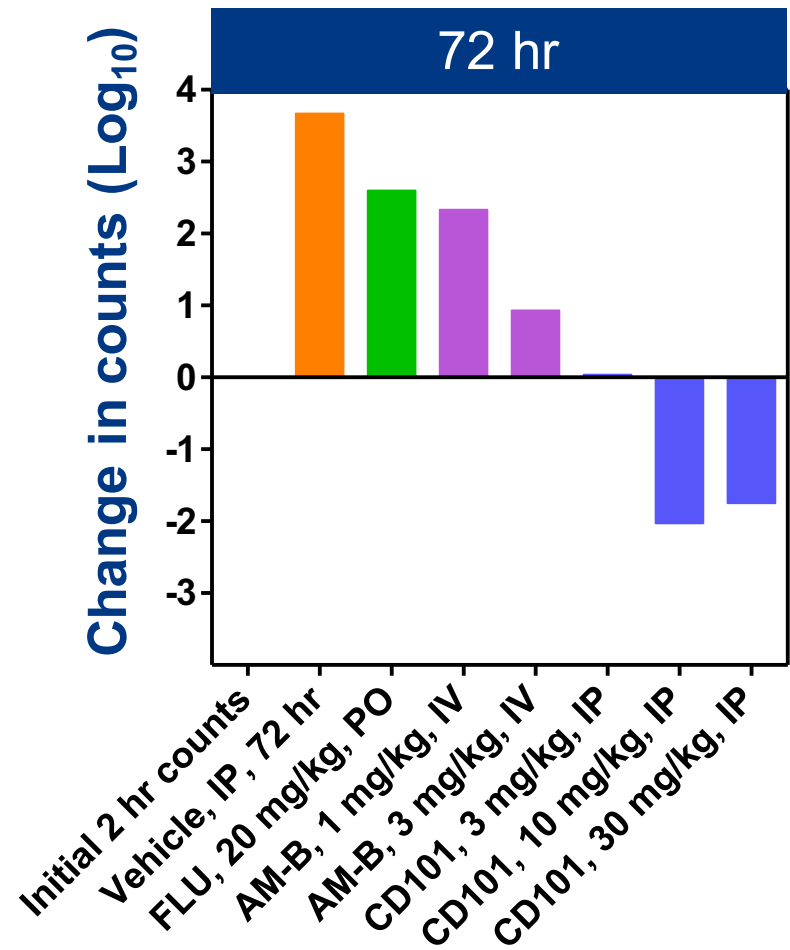
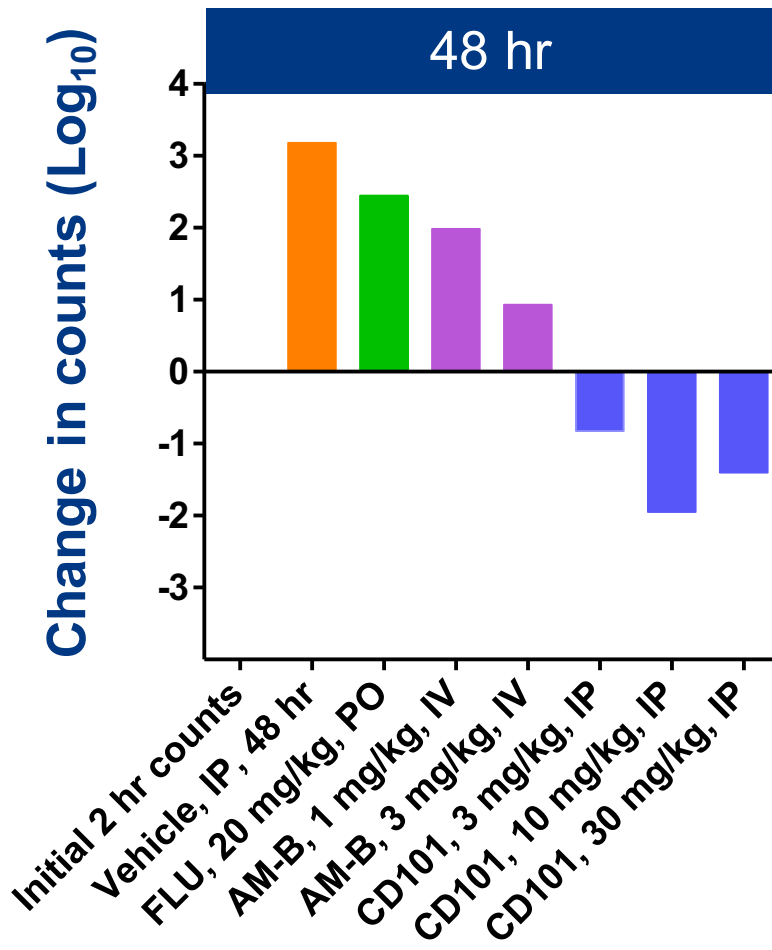
## Efficacy of antifungals - fungal counts



\* ≥99% reduction  
# p < 0.05 vs. vehicle

# Azole-resistant *C. albicans* R357 disseminated infection model

## Efficacy of antifungals - difference in counts



- **CD101, a novel echinocandin, demonstrated efficacy in a disseminated infection model of azole-resistant candidiasis**
- **Efficacy persisted 72 hr consistent with long-acting pharmacokinetics**
- **CD101 treatment resulted in a fungicidal effect**