

in AKI was detected between patients with MER-VAN and with MER-TEI (table). Mortality at 7 and 30 days and resolution of AKI at discharge were similar in all groups.

Table. Comparison of various antibiotic combinations causing AKI

Variable	Combinations		Unadjusted OR (95% CI)	PValue	Adjusted OR (95% CI)	PValue
	TZP-VAN (n=50)	TZP-TEI (n=85)				
AKI	20 (40.0)	17 (20.0)	2.66 (1.22-5.79)	.012	3.21 (1.36-7.57)	.008
Risk	13 (26.0)	12 (14.1)				
Injury	4 (8.0)	3 (3.5)				
Failure	3 (6.0)	2 (2.4)				
	MER-VAN (n=104)	MER-TEI (n=140)				
AKI	25 (24.0)	34 (24.3)	0.98 (0.54-1.78)	.96	1.20 (0.62-2.32)	.574
Risk	13 (12.5)	17 (12.1)				
Injury	8 (7.7)	12 (8.6)				
Failure	4 (3.8)	5 (3.6)				
	TZP-VAN (n=50)	MER-VAN (n=104)				
AKI	20 (40.0)	25 (24.0)	2.10 (1.02-4.34)	.041	2.28 (1.008-5.18)*	.048
Risk	13 (26.0)	13 (12.5)				
Injury	4 (8.0)	8 (7.7)				
Failure	3 (6.0)	4 (3.8)				

Conclusion. TZP causes increased nephrotoxicity when combined with VAN. Combination with TEI may offset this side effect. Additionally, the higher AKI incidence with TZP-VAN than MER-VAN may suggest a particular nephrotoxic synergy between TZP and VAN. Randomized controlled trials should confirm this observation.

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1412. Caspofungin and Anidulafungin Behave as Fungistatic Agents Against *Candida auris*

Catiana Dudiuk, PhD^{1,2}; Indira Berrio, MD, MSc^{3,4}; Laura Theill, PhD^{1,2}; Soraya Morales-Lopez, PhD^{5,6}; Soraya Salcedo, MD, MSc⁷; Jose Rodriguez, MD^{8,9}; Soledad Gamarra, PhD^{1,2} and Guillermo Garcia-Effron, PhD^{1,2}; ¹Laboratorio de Micología y Diagnóstico Molecular-Cátedra de Parasitología y Micología-Facultad de Bioquímica y Ciencias Biológicas-Universidad Nacional del Litoral, Santa Fe, Argentina, Santa Fe, Argentina, ²Consejo Nacional de Investigaciones Científicas y Tecnológicas (CONICET), CCT-Santa Fe, Argentina, Santa Fe, Argentina, ³Medical and Experimental Mycology Group, Corporación para Investigaciones Biológicas (CIB), Medellín, Colombia, ⁴Hospital general de Medellín "Luz Castro de Gutiérrez" ESE, Medellín, Colombia, ⁵Universidad Popular del Cesar, Valledupar, Colombia, Valledupar, Colombia, ⁶Laboratorios Nancy Flórez García S.A.S, Valledupar, Colombia, Valledupar, Colombia, ⁷Clinica General del Norte, Barranquilla, Colombia, ⁸Hospital Rosario Pumarejo Lopez, Valledupar, Colombia, ⁹Centro de Investigaciones Microbiológicas del Cesar-CIMCE Ltda, Valledupar, Colombia, Valledupar, Colombia

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Background. *Candida auris* is an emerging multidrug-resistant nosocomial pathogen responsible for outbreaks around the world. It is associated with therapeutic failure and high mortality rates. Echinocandins are the empiric treatment choice for *C. auris* infections. However, clinical reports show that some patients respond poorly to this therapy. The aim of this study was to determine the in vitro activity of Caspofungin and Anidulafungin against *C. auris* by time-kill curves method.

Methods. Twenty *C. auris* strains were studied. They were isolated from patients with proven invasive fungal infection. Susceptibility testing was performed following the Clinical and Laboratory Standards Institute (CLSI) M27-A3 and S4 documents. Time-killing experiments were conducted for 10 of the 20 isolates (in duplicate on 2 separate days) using RPMI-1640 buffered with MOPS. Caspofungin and anidulafungin tested concentrations were 0.12, 0.25, 0.50, 1.00 and 8.00 µg/mL. The inoculum was adjusted to 1×10^5 CFU/mL using a Neubauer chamber. A 0.05 mL aliquot of each dilution was taken at different time points (0, 2, 4, 6, 8, 10, 24 and 48 hours). These aliquots were serially diluted in sterile water, spread onto Sabouraud plates and incubated at 35°C to determine the numbers of CFU per milliliter. The killing kinetics and the fungicidal activity were analyzed by fitting the mean data at each time point to an exponential equation: $N_t = N_0 \times e^{-kt}$ (N_t viable yeasts at time t ; N_0 starting inoculum; K killing rate; t incubation time).

Results. Anidulafungin and caspofungin MICs geometric means were 1.68 µg/mL (range: 0.5–8.0 µg/mL) and 2.55 µg/mL (range 0.25–8.0 µg/mL), respectively. None of the drugs were able to reach fungicidal activity (no 99.9% inhibition). The mean time to reach 50% growth reduction were 1.74 ± 0.45 hours and 5.30 ± 2.81 hours for the MIC values of each strain for anidulafungin and caspofungin, respectively

Conclusion. The tested echinocandins showed no in vitro fungicidal activity against *C. auris* at concentrations reached in serum despite strain's MICs. Caspofungin exhibited a significant lowest killing rate.

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1413. A Phase IIa Efficacy, Safety, Tolerability and Pharmacokinetic (PK) Study of Encocleated Amphotericin B in Patients with Mucocutaneous (Esophageal, Oropharyngeal, Vulvovaginal) Candidiasis Who are Refractory or Intolerant to Standard Non-Intravenous Therapies

Lilian Kibathi, PharmD¹; Parag Kumar, PharmD¹; Michail Lionakis, MD, Sc.D²; Amanda Urban, CRNP³; Elise Ferre, PA-C, MPH²; Maryellen McManus, RN, MPH³; Benjamin Colton, PharmD¹; Chris Lambros, PhD²; Ruying Lu, BS⁴; Raphael Mannino, PhD¹; Edmund Tramont, MD, FIDSA² and Alexandra F. Freeman, MD¹; ¹Clinical Center, Pharmacy Department, National Institutes of

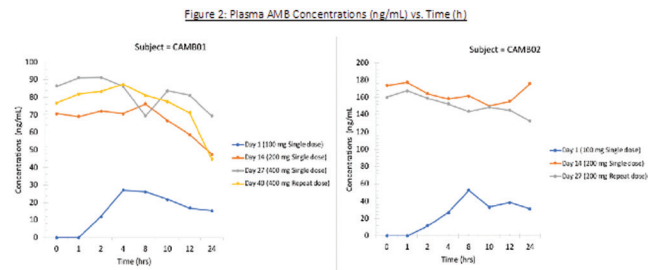
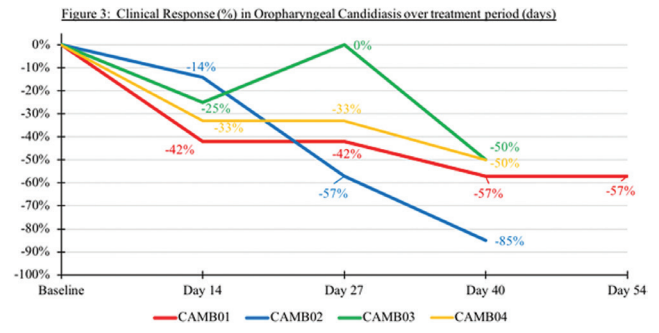
Health, Bethesda, Maryland, ²National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, ³Medical Science & Computing, Bethesda, Maryland, ⁴Matinas BioPharma, Inc., Bedminster, New Jersey

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Background. Current oral therapeutic options for chronic mucocutaneous candidiasis (CMC) are often associated with resistance and toxicity. Amphotericin B (AMB) has broad fungicidal activity and markedly resists emergence of resistance but requires parenteral administration and monitoring for significant nephrotoxicity, which worsens with chronic treatment. Encocleated amphotericin B (CAMB) is a novel oral formulation of AMB. In animal models, CAMB demonstrates antifungal activity with similar efficacy as intraperitoneal AMB deoxycholate, but without the associated toxicity. This on-going patient volunteer study assesses the efficacy, safety, tolerability and PK of CAMB in patients with CMC who are refractory or intolerant to standard oral azole antifungals.

Methods. Four patients have completed the clinical protocol treatment period: 3 patients with STAT3 deficient Hyper IgE syndrome and CMC, and one patient with chronic esophageal candidiasis. Eligible patients were dose escalated (Figure 1), with option of enrolling in an extension phase. Serial plasma PK samples were collected over 24 hours over the study period, with data available from two patients (Figure 2).



Results. CAMB was well tolerated by all four patients, and all are currently on the extension phase (Figure 3). There was significant improvement in clinical severity symptom scores of esophageal and oropharyngeal symptoms; CAMB01 achieved reduction in clinical symptoms by 57% (800 mg/day), CAMB02 by 85% (400 mg/day), CAMB03 50% (800 mg/day) and CAMB04 50% (800 mg/day). CAMB02 maintained higher plasma PK exposure throughout the study compared with CAMB01, a possible explanation for clinical response at a lower 400 mg/day dose. Reported adverse events were grade 1, mostly nausea and dizziness. There were no signs of liver, kidney or hematologic toxicity in any of the patients, with CAMB01 and CAMB02 receiving study drug for ~1 year.

Conclusion. CAMB was well tolerated in patient volunteers with long-standing symptomatic azole-resistant CMC. All four patients have met the primary endpoint of achieving > 50% clinical response. CAMB is a promising oral therapy for patients with history of CMC, with potential use in treatment and prophylaxis of invasive fungal infections.

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1414. Inoculum Effect of Piperacillin/Tazobactam Concentration on Emergence of Resistance in *Klebsiella aerogenes*

Marco Custodio, PharmD¹; Beverly Anderson, BA¹; Daniel Sanchez, BS¹; Keenan Ryan, PharmD, PhC²; Carla Walraven, PharmD, MS² and Renee-Claude Mercier, PharmD³; ¹University of New Mexico, Albuquerque, New Mexico, ²University of New Mexico Health Sciences Center, Albuquerque, New Mexico, ³University of New Mexico College of Pharmacy, University of New Mexico College of Pharmacy, Albuquerque, New Mexico

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