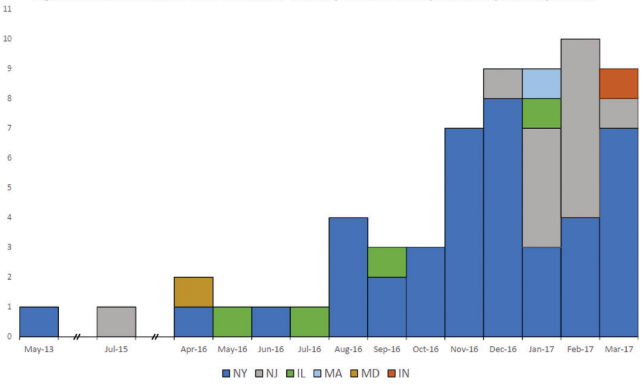
Figure: Number of clinical cases of *Candida auris* reported to CDC by state, May 2013-April 2017



Disclosures. **All authors:** No reported disclosures.

145. Assessment of *Candida auris* Response to Antifungal Drugs Using Time–Kill Assays and an Animal Model

Ronen Ben-Ami, MD[1]; Liat Ashkenazi, MD[2]; Judith Berman, PhD[3]; Nuphar Korolker, MSc[4] and Anna Novikov, MSc[5]; [1]Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel; Infectious Diseases, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, [2]Schneider Medical Center, Petah Tiqva, Israel, [3]Faculty of Life Sciences, Tel Aviv University, Tel Aviv, Israel, [4]Tel Aviv University, Tel Aviv, Israel and [5]Infectious Diseases Unit, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

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Background. *Candida auris* is an emerging nosocomial pathogen that is resistant to Fluconazole and variably susceptible to other systemic drug classes. Treatment with echinocandins has been recommended based on MICs in the susceptible range, but supporting in vivo data is lacking.

Methods. We tested the MIC of *C. auris* strains ($n = 12$) to fluconazole, voriconazole, posaconazole. anidulafungin, amphotericin B and flucytosine. Representative *C. auris* strains from Israel and South Africa, and a reference *C. albicans* strain were analysed using time–kill curve assays. Fungicidal activity was defined as reduction of ≥3 log from baseline CFU/ml. Response to caspofungin treatment was assessed in BALB/c mice immunosuppressed with cyclophosphamide and inoculated with 7×10^7 *C. auris* cells by tail vein injection. Mice were treated from day +1 to day +7 with caspofungin (IP) at doses of 1 or 5 mg/kg and compared with sham-treated controls. Survival was assessed daily. Kaplan-Meier survival analyses were performed and treatment arms were compared using the log-rank test.

Results. Drug susceptibility results (MIC50 and MIC90) were: fluconazole, 64 and 128 mg/l; voriconazole, 0.5 and 24 mg/l; posaconazole, 0.5 and 27 mg/l; anidulafungin, 0.03 and 0.06 mg/l; amphotericin B, 2 and 8 mg/l; flucytosine, 0.3 and 1 mg/l. Time–kill curve analyses showed log reduction from baseline CFU concentration of −3.0 to −2.8 for fluconazole (MIC ×1), 5.6–6.1 for amphotericin B (MIC ×4) and −0.4 to −0.9 for caspofungin (MIC ×16), consistent with fungicidal activity of amphotericin B and weak fungistatic activity of caspofungin. In the mouse model, survival rate was similar with sham treatment (33%) and treatment with caspofungin 1 mg/kg/day (44%) and 5 mg/kg/day (22%), $P = 0.7$.

Conclusion. Despite generally low MIC, caspofungin has only mild fungistatic activity on *C. auris* and no effect on survival in a mouse infection model. Amphotericin B has fungicidal activity against *C. auris*.

Disclosures. **All authors:** No reported disclosures.

146. Pharmacodynamic Optimization for the Treatment of Invasive *Candida auris* Infection

Alexander J. Lepak, MD[1]; Miao Zhao, MS[1]; Elizabeth Berkow, PhD[2]; Shawn Lockhart, PhD[2] and David R. Andes, MD, FIDSA[3]; [1]Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, [2]Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, [3]University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

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Background. *Candida auris* is an emerging, nosocomial multidrug-resistant threat with high treatment failure rate and mortality. The optimal antifungal agent to use and susceptibility breakpoints are based on limited clinical data.

Methods. Nine clinical *C. auris* strains were used. MICs were determined by CLSI standards. Drug treatment studies consisted of: fluconazole (FLC) dose range 0.78–200 mg/kg/12 h, micafungin (MFG) dose range 0.3125–80 mg/kg/24 h, or amphotericin B deoxycholate (AMB) dose range 0.0.78–20 mg/kg/24 hours. Plasma PK was previously determined in the murine model for all three drugs. A 96 h neutropenic murine model of invasive candidiasis (IC) was used for all studies. The Emax Hill equation was used to model the dose–response data to PK/PD index AUC/MIC (FLC and MFG) and Cmax/MIC (AMB). The static and 1 log kill doses (when achieved) and the associated PK/PD targets (AUC/MIC or Cmax/MIC) were determined and compared with previous murine IC studies with *C. albicans*, *C. glabrata*, and *C. parapsilosis*.

Results. MIC range: FLC 2–256 mg/l, MFG 0.125–4 mg/l, and AMB 0.38–6 mg/l. Dose-dependent activity was observed with all three drugs. Net stasis was achieved against seven strains for FLC, eight strains for MFG, and eight strains for AMB. However, MFG performed significantly better than comparators for cidal endpoints. A 1 log kill endpoint was achieved in eight strains for MFG, whereas this endpoint was only achieved in one strain for FLC and three strains for AMB. PK/PD analyses demonstrated a strong relationship between AUC/MIC and treatment outcome for FLC (R^2 0.61) and MFG (R^2 0.77); and Cmax/MIC and treatment outcome for AMB (R^2 0.64). The median static dose and 1 log kill dose (MFG only) and associated AUC/MIC or Cmax/MIC values are shown (Table).

	Stasis		1 log kill	
Drug	Dose (mg/kg/24 hours)	AUC/MIC or [Cmax/MIC]	Dose (mg/kg/24 hours)	AUC/MIC
FLC	107	26.3		
MFG	1.25	53.7	3.36	130
AMB	3.86	[0.87]		

Conclusion. MFG was the most potent drug over the dose range achieving up to 2 log kill against eight of nine strains. PK/PD targets for *C. auris* against FLC and AMB were similar to other *Candida* species; however, MFG targets were ≥20-fold lower than *C. albicans*, *C. glabrata*, and *C. parapsilosis*. Using the median stasis targets and human PK for each drug, resistance thresholds could be 16 mg/l for FLC, 2–4 mg/l for MFG, and 1–2 mg/l for AMB.

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147. Risk Predictive Model for 90-Day Mortality in *Candida* Bloodstream Infections

Charlotte Lin, BA[1]; Alyssa Kronen, BA[2]; Kevin Hsueh, MD[3]; William Powderly, MD[4] and Andrej Spec, MD[5]; [1]Infectious Disease, Washington University School of Medicine, St. Louis, Missouri, [2]Washington University School of Medicine, St. Louis, Missouri, [3]Infectious Disease, Washington University in St louis, St Louis, Missouri, [4]Division of Infectious Disease, Washington University in St. Louis, St. Louis, Missouri, [5]Infectious Disease, Washington University, St Louis, Missouri

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Background. *Candida* bloodstream infections (CBSI) continue to be associated with high mortality, despite changes in antifungal treatment and diagnostics.

Methods. All patients age 18 or greater with a first episode of CBSI by blood culture from 1/2002 to 1/2015, admitted to Barnes-Jewish Hospital, a tertiary referral hospital in St. Louis, MO, were included. We collected data on demographics, comorbidities, laboratory values, vital signs, indwelling devices, and medical treatments of interest from the electronic medical record. We analyzed the potential predictor variables using univariate logistic regression. Variables associated with mortality were considered for model inclusion. The final model was built using multivariable binary logistic regression. A predictive equation was created, and a receiver–operator curve (ROC) was calculated to determine the appropriate cut-off points and c-statistic.

Results. Of the 1873 episodes of CBSI identified, 789 (42%) resulted in death in 90 days. The variables included in this model were age (40–49: OR 0.463, 95% CI 0.291–0.736; 50–69: 0.542, 0.342–0.860; ≥70: 0.560, 0.400–0.785); history of CAD (1.616, 1.171–2.230), chronic liver disease (2.247, 1.327–3.806); maximum heart rate (1.496, 1.126–1.989) and temperature (0.537, 0.408–0.708); AST (1.817, 1.343–2.459) and platelet count (1.563, 1.178–2.073); the presence of ventilator (1.847, 1.321–2.582), urinary catheter (1.365, 1.008–1.847), two or more central lines (1.658, 1.020–2.694); removal of lines after positive culture (0.259, 0.181–0.370); ophthalmology consult during admission (0.441, 0.329–0.592); thoracentesis/chest tube (3.827, 1.550–9.448); diagnosis of secondary malignancy (2.131, 1.488–3.053); whether antimetabolites (2.119, 1.353–3.318), dapsone (4.507, 1.450–14.012), linezolid (1.605, 1.059–2.435), quinolones (1.384, 0.998–1.920) were ordered 90 days before positive culture. An ROC curve was calculated with an internal c-statistic of 0.806.

Conclusion. We created a risk predictive model for 90-day mortality in patients with CBSI, with 81% probability of predicting mortality. This model can lead to development of point-of-care applications to aid decision-making regarding escalation/de-escalation of care.

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148. Time Trends in the Burden of Hospitalizations with Invasive Aspergillosis in the United States, 2004–2013

Marya D. Zilberberg, MD, MPH[1]; Rachel Harrington, BA[2]; James Spalding, PharmD, MS, MBA[3] and Andrew F. Shorr, MD, MPH[4]; [1]Evimed Research Group, LLC, Goshen, Massachusetts, [2]Former Employee of Astellas Pharma Global Development, Inc., Northbrook, Illinois, [3]Astellas Pharma Global Development, Inc., Northbrook, Illinois, [4]Washington Hospital Center, Washington, DC