2400. Activity of a Long-Acting Echinocandin, Rezafungin, Tested Against Invasive Fungal Isolates Collected Worldwide Michael A. Pfaffer, MD; Shawn A. Messer, MS-MT; Paul R. Rhomberg, BS; Beth A. Schaefer, BS and Marianna Castanheira, PhD; JMI Laboratories, Inc., North Liberty, Iowa
Session: 250. Treatment of AMR Infections Saturday, October 6, 2018: 12:30 PM

Background. Echinocandins are important agents for treating invasive fungal infections. We evaluated the activity of rezafungin (RZF; previously CDI01), an echinocandin with extended half-life, and compared using CLSI broth microdilution methods against 719 invasive fungal isolates collected worldwide during 2017.

Methods. Susceptibility tests were conducted on 616 Candida spp. (6 species), 25 C. neoformans (25; 18 A. fumigatus (AFU), 60 A. fumigatus (AFU) for RZF; anidulafungin, caspofungin, micafungin, and azoles. CLSI clinical breakpoint (CBP) and epidemiological cutoff value (ICV) interpretive criteria were applied.

Results. RZF inhibited 100.0% of C. albicans (CA) isolates, 96.3% of C. tropicalis (CT), 93.4% of C. glabrata (CG), 100.0% of C. krusei, and 100.0% of C. dubliniensis at ≤0.12 µg/mL. All but 2 (116/118 [98.3%]) C. parapsilosis (CP) isolates were inhibited by RZF at ≤52 µg/mL. Resistance to fluconazole was detected among 10.7% of CG, 10.2% of CP, 1% of CT, and 0.7% of CA. The activity of RZF against these 6 Candida spp. was similar to that of the other echinocandins, the vast majority of which were susceptible/wild type (WT) using CBP/ECV. Fluconazole and other triazoles displayed good activity against CNEO whereas echinocandins, including RZF, displayed limited activity against CNEO isolates (MIC90 ≥8 µg/mL). Echinocandins displayed good activity against ASF and AFI, and RZF activity was similar to that of anidulafungin, caspofungin, and micafungin. All isolates displayed WT MIC values for the mold-a- active azoles.

Conclusion. Rezafungin was as active as other echinocandins against common fungal organisms recovered from invasive fungal infections. The extended half-life and stability of rezafungin is very desirable for prevention and treatment, especially in patients who could be discharged on outpatient therapy.

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2401. Risk Factors for Antimicrobial Resistance in Invasive Pneumococcal disease (IPD) in Toronto, Canada, 2012–2017 Thomas Fear, MD; Karen Green, MSc, RN; Agron Plevneshi, BSc; Jeff Li, BSc; William Fullar, MD, PhD; Paul Schaefer, MD, FCFP; James Garbutt, MD, FRCP(C); Andrew Armstrong, MD, FRCP(C); Toronto Invasive Bacterial Diseases Network; 1Internal Medicine, University of Toronto, Toronto, ON, Canada; 2Mount Sinai Hospital, Toronto, ON, Canada; 3Microbiology, Sinai Health System, Toronto, ON, Canada; 4Laboratory Medicine and Pathobiology, University of Toronto; Toronto, ON, Canada
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Background. Several studies have documented factors predictive of antimicrobial resistance (AMR) in invasive pneumococcal disease(IPD). However, the implementation of routine pediatric PCV programs, antimicrobial stewardship, and increasing immunocompromised in populating might be expected to change such factors. We report on predictive factors for AMR in IPD from 2012 to 2017.

Methods. TIBERON performs population-based surveillance for IPD in Toronto/ Peel (pop 4.5M). IPD cases are reported to a central office and one isolate/case is sero- typed and has antimicrobial susceptibility testing performed by broth microdilution to CLSI standards.

Results. 2459 cases of IPD were identified from January 2012 to December 2017. Overall rates of resistance to penicillin, macrolides, fluoroquinolones, and TMP-SMX were relatively stable over the course were stable over the study. Risk factors for infection with resistant to penicillin at meningitis breakpoints as opposed to penicillin- susceptible pneumococci were current residence at nursing home (odds ratio [OR], 3.30; P = 0.006), immune compromise status (OR, 1.41; P = 0.012), HIV infection (OR, 2.13; P = 0.016), history of receiving PPV23 vaccine (OR 1.38; P = 0.007). Infection with TMP-SMX-resistant pneumococci was associated with HIV infection (OR, 3.2; P = 0.001) and current residence in a nursing home (OR 2.4, P = 0.002). Infection with macrolide-resistant isolates was associated with any use of macrolide 3 months prior to infection (OR, 3.24; P = 0.001), or macrolide treatment failure of the current episode (OR, 6.64; P = 0.003). Infection with levofloxacin-resistant pneumococci was associated with current residence in a nursing home (OR, 13.7; P < 0.001), and fluoroquinolone treatment failure of the current episode (OR 49.4, P = 0.0034).

Conclusion. Previous same class antibiotic exposure remains a major predictive factor for macrolide resistance. History of treatment failure is a predictive factor for macrolide and fluoroquinolone failure. HIV infection and immune compromise are risk factors for IPD infection with penicillin resistant pneumococci. Hospital acquisition of infection is no longer a risk factor for fluoroquinolone resistance.

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2402. Daptomycin Pulmonary Eosinophilia: Review of Cases and New Hyperacute Syndromic Presentation Katelyn West, MS; Kimberly Mackay, PharmD and Graeme N. Forrest, MBBS, PhDNA; VA Portland Healthcare System, Portland, Oregon, 2Pharmacy, VA Portland Healthcare System, Portland, Oregon, 3Division of Infectious Diseases, Veterans Affairs Portland Health Care System, Portland, Oregon, 4Section of Infectious Disease, Department of Medicine, Oregon Health & Science University, Portland, Oregon
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Background. Daptomycin pulmonary eosinophilia (DPE) has been described as a rare event. Since the Food and Drug Administration (FDA) first described the syn- drome in 2010, there have been over 30 reports of daptomycin-induced DPE from events that began within 48 days of starting daptomycin to as late as 20 months after initiation of therapy. DPE may be underreported and is associated with doses of 500 mg or 750 mg/kg, with CrCl <35 mL/minute and older age. Of concern are the new cases of hyperacute DPE within 48 hours of re-exposure to daptomycin that we have seen, who had prior low grade eosinophilia. Close monitoring of these factors may be warranted in at risk individuals.

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2403. Comparison of Daptomycin Combination Therapy With Ceftaroline or Oxacillin Against Methicillin-Resistant Staphylococcus aureus (MRSA) Isolates Causing Bacteremic Bacteremia Thomas Fear, MD; Kendall Green, MSc, RN; Agron Plevneshi, BSc; Jeff Li, BSc; William Fullar, MD, PhD; Paul Schaefer, MD, FCFP; James Garbutt, MD, FRCP(C); Toronto Invasive Bacterial Diseases Network; 1Internal Medicine, University of Toronto, Toronto, ON, Canada; 2Mount Sinai Hospital, Toronto, ON, Canada; 3Microbiology, Sinai Health System, Toronto, ON, Canada; 4Laboratory Medicine and Pathobiology, University of Toronto; Toronto, ON, Canada
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Background. Increasing evidence suggests that daptomycin (DAP) demonstrates in vitro synergy in combination with other anti-staphylococcal agents, including cef- taroline (CPT) and oxacillin (OXA), against MRSA. Nevertheless, optimal combina- tion therapy is not yet known.

Methods. Minimum inhibitory concentrations (MICs) for DAP, CPT, and OXA were determined in duplicate by reference broth microdilution methods. We used time-kill analyses (TKA) to test free peak concentrations (IC50) of DAP (8 µg/mL), CPT (16 µg/mL), and OXA (4 µg/mL) alone and in combination among 48 hours of a representative isolate of DAP-resistant MRSA. TKA were performed using 80% of IC50 for DAP alone or in combination with CPT or OXA against 80% and 60% of isolates, respectively. In combination with CPT or OXA against MRSA bloodstream isolates collected from patients with persistent bacteremia despite >7 days of vancomycin treatment. Four patients had a severe and novel hyperacute DPE within 48 hours of a new initiation of daptomycin therapy. All 4 patients had prior exposure to daptomycin in the last 12 months. They presented with hypoxic respiratory failure, abnormal chest x-rays and/or CT chest scans, with preceding systemic fevers and fatigue after the first dose. All had low grade (3–5%) on prior use, and all recovered rapidly with discontinuance of daptomycin.

Conclusion. DPE may be underreported and associated with doses of 500 mg or 750 mg/kg, with CrCl <35 mL/minute and older age. Of concern are the new cases of hyperacute DPE within 48 hours of re-exposure to daptomycin that we have seen, who had prior low grade eosinophilia. Close monitoring of these factors may be warranted in at risk individuals.

Disclosures. All authors: No reported disclosures.