identifications were confirmed at JMI Laboratories. Susceptibility testing was performed according to CLSI broth microdilution methodology, and CLSI (2019) breakpoints were applied where applicable. Other antimicrobials tested included levofloxacin (LEV) and moxifloxacin (MOX; not tested in 2015). Multidrug-resistant (MDR) SPN isolates were categorized as being nonsusceptible (NS) to amoxicillin-clavulanate, erythromycin, and tetracycline; other SPN phenotypes were LEV-NS or penicillin (PEN)-NS. β-Lactamase (BL) presence was determined for HI, HP, and MC.

Results. The activities of the 3 FQs are shown in the table. The most active agent against SPN was DLX, with the lowest $MIC_{50/90}$ values of 0.015/0.03 mg/L. DLX activities were similar when tested against the MDR or PEN-NS for SPN phenotypes. LEV-NS isolates had DLX $MIC_{50/90}$ results of 0.12/0.25 mg/L. DLX was the most active FQ against HI, HP, and MC. BL presence did not affect FQ MIC values for HI or MC; only 2 HP isolates were BL-positive.

Conclusion. DLX demonstrated potent *in vitro* antibacterial activity against SPN, HI, HP, and MC. DLX was active against MDR SPN that were NS to the agents commonly used as treatments for CABP. DLX had excellent activity against LEV-NS SPN. These data support the continued study of DLX as a potential treatment for CABP.

Organism/Phenotype (n)	Delafloxacin $MIC_{50/90}$ (mg/L)	Levofloxacin $MIC_{50/90}$ (mg/L)	Moxifloxacin $MIC_{50/90}$ (mg/L, n[a])
S. pneumoniae (1,975)	0.015/0.03	1/1	≤0.12/0.25 (1,684)
MDR (84)	0.03/0.03	1/2	≤0.12/0.25 (74)
Pen-NS (745)	0.015/0.03	1/1	≤0.12/0.25 (637)
LEV-NS (16)	0.12/0.25	>4/>4	2/4 (13)
H influenzae (1,128)	≤0.001/0.002	≤0.015/0.03	0.03/0.06 (965)
BL-positive (363)	≤0.001/0.002	≤0.015/0.03	0.03/0.06 (318)
H. parainfluenzae (43)	0.008/0.015	0.03/0.12	0.12/0.25 (10)
M. catarrhalis (684)	0.004/0.008	0.03/0.06	0.06/0.06 (598)
BL-positive (589)	0.004/0.008	0.03/0.06	0.06/0.06 (585)

[a]Number of isolates shown for moxifloxacin, not tested in 2015.

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

1583. Eight Years of Sustained Potency and Activity of Oritavancin against Gram-Positive Isolates Causing Bacteremia and Endocarditis in the USA, Including Enterococcal Infections Requiring an Optimized Dosing Strategy for Daptomycin

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Background. Oritavancin (ORI) is a potent lipoglycopeptide with desirable PK/PD parameters for treating serious gram-positive infections. This study assessed the activity of ORI against *Staphylococcus aureus* (SA), *Enterococcus faecalis* (EF), and *E. faecium* (EFM) causing bloodstream infection (BSI), including infective endocarditis (IE) and daptomycin (DAP)- susceptible dose-dependent (SDD) vancomycin-resistant (VRE) subsets. We also evaluated the longitudinal activity of ORI.

Methods. A total of 5,469 SA, 1,157 EF, and 721 EFM were recovered from BSI in 35 US sites (2011–2018). Subsets of SA isolates causing IE (84) and EFM displaying DAP-SDD-VRE phenotypes (230) were included. Identification was confirmed by MALDI-TOF MS and isolates were tested for susceptibility (S) according to CLSI.

Results. Overall, ORI showed similar MIC_{50} (0.03 mg/L) and MIC_{90} results (0.06 mg/L) against MRSA and MSSA (figure) and the SA EC subset (41.7% MRSA; data not shown). Similar findings were noted for ORI tested against EF DAP-S ($MIC_{50/90}$, 0.015/0.06 mg/L) and DAP-SDD ($MIC_{50/90}$, 0.015/0.06 mg/L). ORI MIC values against DAP- and VAN-S EFM ($MIC_{50/90}$, ≤0.008/0.015 mg/L) were at least 8-fold lower than those from DAP-SDD-VRE isolates ($MIC_{50/90}$, 0.06/0.12 mg/L; 31.9% of all EFM), and all EFM were inhibited by ORI at ≤0.25 mg/L. The longitudinal analysis showed MRSA rates varying from 39.7% (2017) to 46.8% (2011), while the annual ORI MIC_{50} and MIC_{90} results were 0.015–0.06 mg/L and 0.03–0.12 mg/L, respectively, against MRSA during the 8-year period. ORI yearly MIC_{50} and MIC_{90} results were 0.015–0.03 mg/L and 0.03–0.12 mg/L against EF, respectively. MIC_{50} and MIC_{90} results of 0.008–0.03 mg/L and 0.03–0.12 mg/L, respectively, were obtained for ORI against the DAP-SDD EF subset each year. ORI MIC_{50} and MIC_{90} results of 0.03–0.06 and 0.06–0.12 mg/L were obtained annually against DAP-SDD-VRE (EFM), respectively.

Conclusion. ORI showed a potent activity against this collection of isolates causing BSI and IE in the USA, including resistant subsets requiring higher dosage regimens when treating serious infections. In addition, ORI maintained a stable potency throughout the 8-year study period with no apparent temporal trends.

Organism / Phenotype	Cumulative % inhibited by oritavancin at:							$MIC_{50/90}$
	0.008	0.015	0.03	0.06	0.12	0.25	0.5	
S. aureus								
MSSA	4.2	40.1	79	95.9	100			0.03/0.06
MRSA	3.6	39.7	77.4	95	99.9	100		0.03/0.06
E. faecalis								
DAP-S	27.5	68.4	88.9	94.4	97.8	99.6	100	0.015/0.06
DAP-SDD	28.9	61.4	77.1	92.8	98.8	100		0.015/0.06
E. faecium								
DAP-S-VSE	85.6	99	100					≤0.008/0.015
DAP-SDD-VRE	4.3	18.3	49.6	82.2	97	100		0.06/0.12

MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; DAP-S, daptomycin susceptible; DAP-SDD, daptomycin susceptible-dose dependent; VSE, vancomycin-susceptible enterococci; VRE, vancomycin-resistant enterococci.

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

1584. Minocycline Activity Against *Stenotrophomonas maltophilia* Isolated From Patients in US Hospitals

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Background. *Stenotrophomonas maltophilia* (SM) has emerged as a common hospital-associated opportunistic pathogen found in immunocompromised and immunocompetent patients. SM is intrinsically resistant to many common drug classes, including carbapenems, cephalosporins, and aminoglycosides. Only 4 antibiotics have CLSI breakpoints for SM: minocycline (MIN), ceftazidime (CAZ), levofloxacin (LVX) and trimethoprim-sulfamethoxazole (TMP-SMX). Minocycline is frequently used to treat SM infections. In this study, we analyzed susceptibilities of SM isolates collected as part of the SENTRY Program. We also examined the frequency of SM isolation from pneumonia in hospitalized patients (PIHP) among all Gram-negative (GN) species.

Methods. From 2014 to 2018, 990 SM isolates were collected from hospitalized patients in 32 US hospitals. Hospitals submitted 1 isolate per patient per infection episode that met local criteria for being the likely causative pathogen and submitted consecutive isolates from pneumonia. Isolates were tested for MIN susceptibility (S) using the CLSI broth microdilution method at JMI Laboratories. Other antimicrobials tested were CAZ, LVX, and TMP-SMX. TMP-SMX was tested 3 of 5 years. All infection types were included in the susceptibility analysis. The prevalence of SM isolates in PIHP during this period was also analyzed.

Results. There were 9,120 GN pathogens isolated from PIHP. The most commonly isolated species was *P. aeruginosa* (34.7%), followed by *Klebsiella pneumoniae* (12.6%), *Escherichia coli* (10.1%), and SM (7.9%). Among the 990 infections caused by SM, PIHP was the most common at 72.4%, followed by bloodstream infections (14.4%) and skin/skin structure infections (6.9%). The %S and $MIC_{50/90}$ values of the 4 antimicrobials tested in this study are shown in the table.

Conclusion. SM was the fourth most frequent cause of GN PIHP in US medical centers. MIN was the most active drug tested against SM with 99.5%S, followed by TMP-SMX (94.7%), and CAZ was the least active with 28.5%S. This study suggests that MIN may be a consideration as a treatment for infections caused by SM, with a very low resistance rate based on CLSI breakpoints.

Table. Activities of MIN and comparator agents when tested against 990 *S. maltophilia* isolates

Antimicrobial agent	No. of isolates	MIC_{50}	MIC_{90}	Range	CLSI[a]		
					%S	%I	%R
Minocycline	990	0.5	2	≤0.06 to >8	99.5	0.3	0.2
Ceftazidime	990	32	>32	0.25 to >32	28.5	10.2	61.3
Levofloxacin	990	1	>4	≤0.12 to >4	77.8	8.9	13.3
Trimethoprim-sulfamethoxazole	609	≤0.5	1	≤0.5 to >4	94.7		5.3

[a] CLSI (2019).

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

1585. Isavuconazonium Sulfate plus Micafungin Improves Survival in an Immunocompromised Murine Model of Disseminated Fusariosis

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Background. Disseminated fusariosis in patients with hematological malignancies is a frequently fatal and emerging invasive mycosis. *Fusarium* spp. are often resistant to safely achievable concentrations of mould active triazoles and amphotericin B. We aimed to determine the efficacy of isavuconazonium sulfate (ISA) alone or in combination with micafungin (MICA) in a murine model of disseminated fusariosis caused by *Fusarium solani.*

Methods. Groups of five 5-week-old Swiss Webster female mice, 20–22 g, were rendered neutropenic by intraperitoneal (IP) injection of cyclophosphamide at 200 mg/kg on day −2 and 150 mg/kg on day +3. Mice were infected with $5 \times 10E^5$ CFU *F. solani* intravenously (IV) via the lateral tail vein on day 0. To prevent bacterial infection, ceftazidime was administered 50 mg/kg/day IP. Therapy began 18 h post-challenge for 6 days. MICA was given at dosages of 10, 5, 2.5 and 1.25 mg/kg IP Q12h combined with ISA 14 mg/kg/day IP. Six groups of mice received ISA orogastrically (OG) Q8h, Q12h and Q24h at 224 mg/kg alone or combined with MICA at 10 mg/kg Q12h IP. Kaplan–Meier survival analysis was performed.

Results. ISA at 14 mg/kg Q12h combined with 10 mg/kg MICA doses resulted in improved survival but with no significant reduction of residual fungal burden compared with monotherapy or other ISA/MICA dose combinations. Improved survival

with dose-escalated oral monotherapy was observed at ISA 224 mg/kg Q12h (50% survival) and Q8h OG (60%) compared with other monotherapy or combination, or untreated groups (18–20%). The residual fungal burden in kidney between monotherapy and combination therapy groups was 5.81 10Log (untreated), 4.03 10Log (ISA 224 mg/kg, OG Q12h), 5.19 10Log (ISA 224 mg/kg Q12h + MICA 10 mg/kg, Q12h), 4.67 10Log (ISA 224 mg/kg, Q24h), and 4.82 10Log (ISA 224 mg/kg Q24h + MICA 10 mg/kg, Q12h).

Conclusion. High doses of isavuconazole (exceeding currently approved human dosages) in combination with micafungin improved survival in experimental murine disseminated fusariosis. Given the excellent safety profile of ISA, exploration of higher dosages that are necessary to achieve this antifungal effect is warranted for successful management of disseminated fusariosis.

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

1586. *In Vitro* Activity of Rifampin, Rifabutin, Rifapentine, and Rifaximin Against Biofilms Formed by Staphylococci Isolated from Prosthetic Joint Infection

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Background. Prosthetic joint infections (PJIs) are serious complications after total joint arthroplasty. *Staphylococcus aureus* and *Staphylococcus epidermidis*, which are proficient biofilm-formers, account for ~60% of PJI cases. Therapy often includes rifampin because of its anti-biofilm activity; the activity of other rifamycins against staphylococcal biofilms is poorly defined. This study evaluated the *in vitro* activity of rifampin, rifabutin, rifapentine, and rifaximin against *S. aureus* and *S. epidermidis* biofilms formed by isolates from patients with PJI.

Methods. 200 staphylococcal isolates were tested (111 *S. aureus* and 89 *S. epidermidis*). All *S. aureus* isolates, and all except 7 *S. epidermidis* isolates, were rifampin susceptible. Rifampin, rifabutin, rifapentine, and rifaximin minimum biofilm inhibitory concentrations (MBICs) and minimum biofilm bactericidal concentration (MBBCs) were determined using a pegged lid microtiter plate assay.

Results. Rifampin-resistant isolates had MBICs and MBBCs ≥16 µg/mL. Results for the rifampin-susceptible isolates are shown. All 193 rifampin-susceptible isolates had rifampin MBICs ≤1 µg/mL (rifampin-susceptible breakpoint for planktonic susceptibility testing), with 1, 2, and 2 isolates having MBICs > 1 µg/mL for rifabutin, rifapentine and rifaximin, respectively. *S. aureus* $MBBC_{50}$ values were 8, 1, 2 and 4 µg/mL for rifampin, rifabutin, rifapentine and rifaximin, respectively. *S. epidermidis* $MBBC_{50}$ values were 2, 0.06, 0.25, and 0.5 µg/mL for rifampin, rifabutin, rifapentine and rifaximin, respectively, for rifampin-susceptible isolates.

Conclusion. Rifabutin and rifapentine, and to a lesser extent, rifaximin, show promising *in vitro* activity against rifampin-susceptible staphylococcal biofilms formed by isolates associated with PJI; studies evaluating *in vivo* activity are warranted.

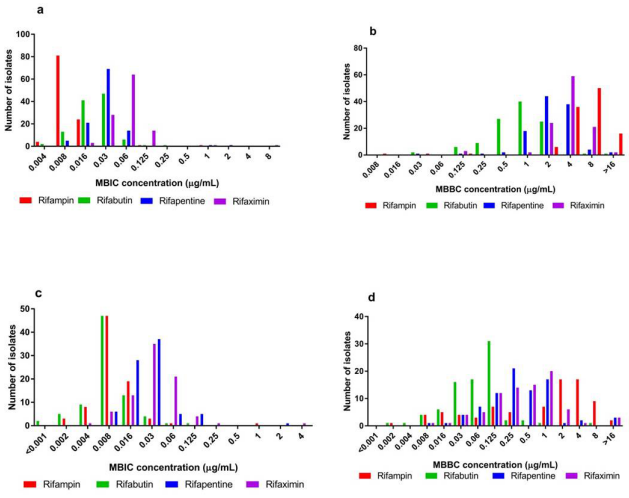

Figure. Distribution of rifampin, rifabutin, rifapentine and rifaximin MBICs and MBBCs for rifampin-susceptible *S. aureus* (a and b, respectively) and *S. epidermidis* (c and d, respectively).

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

1587. Comparative *In Vitro* Antipseudomonal Activity of Ceftolozane/Tazobactam Against *Pseudomonas aeruginosa* Isolates from Children with Cystic Fibrosis

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Background. Ceftolozane/tazobactam (C/T) is a relatively new antipseudomonal cephalosporin combined with a β-lactamase inhibitor approved by the FDA in 2014. The study goal was to evaluate its *in vitro* activity vs. comparator agents against a pre-selected panel of *Pseudomonas* isolates obtained from pediatric patients with cystic fibrosis.

Methods. Clinical *Pseudomonas* isolates from 2 free-standing pediatric centers were obtained from respiratory samples from patients with cystic fibrosis during 2015–2017. Stored isolates were cultured on blood agar (Thermo Fisher Scientific) at 35±1°C for 18–24 hours. A 0.5 McFarland suspension was prepared with Sensititre® demineralized water. Final inocula of 5 × $10E^5$ CFU/mL were prepared in Sensititre® Mueller–Hinton broth. Custom-prepared Sensititre® MIC plates (Thermo Fisher Scientific) containing C/T and 10 comparator antimicrobials were inoculated and incubated at 35±1°C for 18–24 hours. MICs were determined via Sensititre Vizion® system. MIC endpoints (susceptibilities) were interpreted by CLSI (2018) breakpoint criteria.

Results. Data from 83 unique isolates from 2 sites (Missouri: 38 and Texas: 45) for the years 2015–2017 are reported. Overall, 90% of the tested isolates were C/T susceptible (MIC ≤4 µg/mL), while susceptibility for colistin, meropenem, and ciprofloxacin were 93%, 88%, and 86%, respectively (Table 1). C/T exhibited high overall activity (MIC50/90, 1/4 µg/mL) against these *Pseudomonas* isolates. C/T was more active than amikacin, aztreonam, cefepime, ceftazidime, ciprofloxacin, gentamycin, meropenem, piperacillin–tazobactam and tobramycin against tested *Pseudomonas* isolates but less active than colistin.

Conclusion. C/T had broad-spectrum activity and high potency against most *Pseudomonas aeruginosa* from 2 geographically diverse pediatric US medical centers.

Table 1: Susceptibility results against *Pseudomonas aeruginosa* isolates from pediatric patients with cystic fibrosis

Name	% Susceptible	MIC_{50}	MIC_{90}
Amikacin	82	8	64
Aztreonam	69	8	32
Cefepime	83	4	32
Ceftazidime	78	4	32
Ceftolozane/Tazobactam	90	1	4
Ciprofloxacin	86	0.12	8
Colistin	93	2	2
Gentamicin	72	2	64
Meropenem	88	0.25	4
Piperacillin/Tazobactam	81	4	64
Tobramycin	76	1	32

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

1588. Delafloxacin Activity Against *Staphylococcus aureus* with Reduced Susceptibility or Resistance to Methicillin, Vancomycin, Daptomycin, or Linezolid

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Background. Delafloxacin is a recently approved anionic fluoroquinolone antibiotic with broad-spectrum activity against Gram-positive and Gram-negative organisms. The drug has been approved for patients with acute bacterial skin and skin structure infections including those caused by methicillin-resistant *S. aureus*. There is limited data available against methicillin-resistant *S. aureus* blood isolates (MRSABI), vancomycin intermediate strains (VISA), vancomycin-resistant strains (VRSA), daptomycin non-susceptible strains (DNSSA) and linezolid-resistant *S. aureus* (LRSA).

Methods. Antimicrobial activity of delafloxacin, levofloxacin, vancomycin, daptomycin, ceftaroline, and linezolid was determined against recent (2016–2018) MRSABI (110), VRSA (15), VISA (35), DNSSA (40), and LRSA (6). Broth microdilution testing using Mueller–Hinton broth was used to determine minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) according to CLSI guidelines. FDA breakpoints were used to determine delafloxacin susceptibility, and CLSI breakpoints were used for all other antibiotics.

Results. Antimicrobial MIC_{90} expressed in mg/L and (% susceptible)

	MRSABI	*VISA*	*VRSA*	*DNSSA*
Delafloxacin	1 (68)	1 (40)	4 (7)	1 (38)
Levofloxacin	>16 (38)	>16 (9)	> 16 (0)	>16 (15)
Vancomycin	1 (99)	8 (0)	>64 (0)	8 (35)
Daptomycin	1 (96)	4 (26)	1 (100)	4 (0)
Ceftaroline	1 (99)	1 (100)	1 (100)	1 (100)
Linezolid	2 (100)	2 (100)	2 (100)	2 (100)

None of the LRSA were susceptible to delafloxacin or levofloxacin. All strains that were susceptible to the antimicrobial agents above had an MBC that was the same as the MIC or one dilution greater except for linezolid which demonstrated an MBC that was more than eight-fold greater than the MIC. For MRSABI isolates with a levofloxacin MIC ≥ 8 mg/L (55/110) suggesting multiple mutations in the quinolone-resistant determining region, the delafloxacin MIC_{90} was 1 mg/L with a 36.4% susceptibility rate.

Conclusion. Delafloxacin demonstrates superior activity to levofloxacin against recent MRSA blood isolates, VISA, VRSA, and DNSSA.