(ABSSSI; OASIS-1 and OASIS-2) were completed. OMC and comparator efficacies were examined for molecularly characterized baseline pathogens.

***Methods.*** Gram-positive (24) and -negative (17) isolates from the OPTIC (26), OASIS-1 (10) or OASIS-2 (5) trials were selected for characterization. Susceptibility testing and interpretation was performed by CLSI methods. Gram-positive isolates were selected based on tetracycline and/or macrolide, lincosamide, streptogramin$_B$ ($MLS_B$) phenotypes, and tetracycline-nonsusceptible (NS) Gram-negative isolates were selected. Isolates were subjected to next-generation sequencing followed by screening for known tetracycline and/or $MLS_B$ genes. The efficacy endpoint was investigator's assessment of clinical response at post therapy evaluation (PTE).

***Results.*** All *S. aureus* (eight isolates) exhibited a doxycycline-NS phenotype (MIC, 8–16 µg/mL) and OMC MIC values of 0.25–0.5 µg/mL. All *S. aureus* carried *tet*(M), except one isolate with *tet*(K), and one isolate with *tet*(M) and *tet*(L). All but one *S. pneumoniae* (16 isolates; OMC MIC, 0.03–0.06 µg/mL) carried $MLS_B$ genes, while tetracycline- and doxycycline-NS isolates (12) had *tet*(M). *E. coli* (eight isolates; OMC MIC, 0.5–2 µg/mL), *E. cloacae* (two isolates; OMC MIC, 2 µg/mL), and *K. pneumoniae* (six isolates; OMC MIC, 2–16 µg/mL) carried tetracycline efflux-pump genes, *tet*(A) and/or *tet*(B), *tet*(D), and *tet*(A), respectively. *tet* genes were not detected in one *K. pneumoniae* (OMC MIC, 8 µg/mL). Clinical success was noted in 37/41 (90.2%) patients. Two linezolid-treated patients with *S. aureus* (OMC MIC, 0.25 µg/mL) from OASIS-1 and one OMC-treated patient from OPTIC with *E. coli* (OMC MIC, 2 µg/mL) had indeterminate PTE responses. One OMC-treated patient from OPTIC with *K. pneumoniae* (OMC MIC, 8 µg/mL) was a clinical failure at PTE.

***Conclusion.*** This study expands on OMC efficacy data analysis among patients infected with tetracycline–NS pathogens. These results indicate that OMC *in vivo* efficacy is not affected by tetracycline and/or $MLS_B$ resistance mechanisms.

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### 1365. *In Vitro* Activity of Lefamulin (LEF) Against Bacterial Pathogens Causing Community-Acquired Bacterial Pneumonia (CABP): SENTRY Surveillance 2016 Results From Asia-Pacific (APAC) and Latin America (LA)

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***Background.*** LEF, a novel pleuromutilin antibiotic for IV and oral use, recently completed a phase 3 trial for the treatment of CABP in adults where it demonstrated noninferiority to moxifloxacin ± linezolid. LEF selectively inhibits bacterial translation. This study investigated the activity of LEF and comparators against contemporary bacterial respiratory pathogens collected from APAC and LA.

***Methods.*** Unique isolates were collected from patients with pneumonia/respiratory ($n$ = 551), blood stream ($n$ = 169), skin and soft tissue ($n$ = 244), and other ($n$ = 55) infections in seven countries in APAC ($n$ = 587) and four countries in LA ($n$ = 432). LEF and comparators were tested by CLSI broth microdilution methods, and susceptibility was determined using CLSI (2018) breakpoints.

***Results.*** In both APAC and LA, LEF showed potent *in vitro* activity against this collection of respiratory pathogens, with 100% of *Streptococcus pneumoniae* inhibited at ≤0.25 µg/mL. *S. pneumoniae* isolates were largely susceptible to moxifloxacin (98.2% APAC, 100.0% LA), amoxicillin/clavulanic acid (84.3% APAC, 89.4% LA), and ceftriaxone (85.2% APAC, 93.6% LA), but less susceptible to azithromycin (56.6% APAC, 68.1% LA) and penicillin (48.2% APAC, 67.0% LA). LEF was also active against *Staphylococcus aureus* with 99.6% of all isolates from both APAC and LA being inhibited at 0.25 µg/mL. 29.5% of methicillin-resistant *S. aureus* in APAC and 24.7% in LA showed particularly high resistance rates to erythromycin (59.3% APAC, 64.2% LA), moxifloxacin (49.4% APAC, 53.7% LA), and clindamycin (39.5% APAC, 59.7% LA). 98.2% and 97.9% of *Haemophilus influenzae* (in APAC and LA, respectively) were inhibited at LEF ≤2 µg/mL, and 100.0% of *Moraxella catarrhalis* were inhibited at LEF ≤0.12 µg/mL in both APAC and LA. Both organisms were largely susceptible to the comparators, except for ampicillin (49.1% and 74.5% susceptible among *H. influenzae* in APAC and LA, respectively) and trimethoprim/sulfamethoxazole (54.4% and 68.1% susceptible among *H. influenzae*) (figure).

***Conclusion.*** In APAC and LA, LEF was highly active against pathogens collected from CABP patients in 2016, and its activity was not affected by resistance to other antibiotic classes. These data support the ongoing development of LEF for the treatment of CABP.

**$MIC_{50/90}$ of Lefamulin and Comparators**

| | $MIC_{50}$ / $MIC_{90}$ (µg/mL) | | | | |
|---|---|---|---|---|---|
| Organisms (No. of Isolates) | Lefamulin | Amoxicillin-Clavulanic Acid | Azithromycin | Moxifloxacin | Levofloxacin |
| ***Asia-Pacific*** | | | | | |
| *S. pneumoniae* (226) | 0.06 / 0.12 | 0.06 / >4 | 0.06 / >32 | 0.12 / 0.25 | 1 / 1 |
| Penicillin susceptible* (192) | 0.06 / 0.12 | ≤0.03 / 2 | 0.06 / >32 | 0.12 / 0.25 | 1 / 1 |
| Penicillin nonsusceptible† (34) | 0.06 / 0.12 | >4 / >4 | >32 / >32 | 0.12 / 2 | 1 / >4 |
| *S. aureus* (275) | 0.06 / 0.06 | ND | 0.5 / >32 | ≤0.06 / 2 | 0.25 / >4 |
| MRSA (81) | 0.06 / 0.12 | ND | >32 / >32 | 1 / >4 | >4 / >4 |
| *H. influenzae* (57) | 0.5 / 1 | 1 / 8 | 1 / 2 | 0.03 / 0.03 | 0.015 / 0.03 |
| *M. catarrhalis* (29) | 0.06 / 0.12 | 0.12 / 0.25 | 0.015 / 0.03 | 0.06 / 0.06 | 0.03 / 0.06 |
| ***Latin America*** | | | | | |
| *S. pneumoniae* (94) | 0.06 / 0.12 | ≤0.03 / 4 | 0.06 / >32 | 0.12 / 0.25 | 1 / 1 |
| Penicillin susceptible* (86) | 0.06 / 0.12 | ≤0.03 / 0.25 | 0.06 / >32 | 0.12 / 0.25 | 1 / 1 |
| Penicillin nonsusceptible† (8) | 0.06 / – | >4 / – | >32 / – | 0.12 / – | 1 / – |
| *S. aureus* (271) | 0.06 / 0.06 | ND | 0.5 / >32 | ≤0.06 / 2 | 0.25 / >4 |
| MRSA (67) | 0.06 / 0.12 | ND | >32 / >32 | 2 / >4 | >4 / >4 |
| *H. influenzae* (47) | 0.5 / 1 | 0.5 / 2 | 0.5 / 2 | 0.03 / 0.03 | 0.015 / 0.03 |
| *M. catarrhalis* (20) | 0.06 / 0.12 | 0.12 / 0.25 | 0.03 / 0.03 | 0.06 / 0.06 | 0.06 / 0.06 |

MRSA=methicillin-resistant *Staphylococcus aureus*; ND=not determined.
*Penicillin MIC≤2 µg/mL; †Penicillin MIC≥4 µg/mL for the nonmeningitis breakpoint.

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### 1366. *In Vitro* and *In Vivo* Activity of Cefiderocol against *Stenotrophomonas maltophilia* Clinical Isolates

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***Background.*** Cefiderocol (S-649266, CFDC) is a novel siderophore cephalosporin against Gram-negatives, including carbapenem (CR)-resistant strains. Its spectrum includes both the Enterobacteriaceae but also nonfermenters, including *Stenotrophomonas maltophilia*—an opportunistic pathogen with intrinsic resistance to carbapenem antibiotics. In this study, *in vitro* activity and *in vivo* efficacy of CFDC and comparators against *S. maltophilia* were determined.

***Methods.*** MICs of CFDC and comparators (trimethoprim/sulfamethoxazole (TMP/SMX), minocycline (MINO), tigecycline (TGC), ciprofloxacin (CPFX), cefepime (CFPM), meropenem (MEPM), and colistin (CL)) were determined by broth microdilution method as recommended by CLSI. The MIC against CFDC was determined using iron-depleted cation-adjusted Mueller–Hinton broth. *In vivo* efficacy of CFDC, CFPM, ceftazidime–avibactam (CAZ/AVI), MEPM, and CL was evaluated using neutropenic murine systemic infection model caused by strain SR21970. The 50% effective doses ($ED_{50}$s) were calculated by the logit method using the survival number at each dose 7 days after infection.

***Results.*** $MIC_{90}$ of CFDC and comparators against the 216 clinical isolates from global countries collected in SIDERO-CR 2014/2016 study are shown in the table. CFDC, TMP/SMX, MINO, and TGC showed good activity with $MIC_{90}$ of 0.5, 0.25/4.75, 1, and 2 µg/mL, respectively. CFDC, MINO, and TGC inhibited growth of all tested strains at ≤1, ≤4, and ≤8 µg/mL although two strains showed resistance to TMP/SMX. MICs of CFPM, CAZ/AVI, MEPM, and CL were ≥32 µg/mL. The $ED_{50}$ of CFDC against *S. maltophilia* SR21970 with MIC of 0.125 mg/mL was 1.17 mg/kg/dose. Conversely, MICs of CFPM, CAZ/AVI, MEPM/CS, and CL against SR21970 were 32 µg/mL or higher, and $ED_{50}$s were >100 mg/kg/dose, showing that CFDC had potent *in vivo* efficacy against *S. maltophilia* strain which was resistant to other antibiotics.

| | MIC Range (µg/mL) | $MIC_{50}$ (µg/mL) | $MIC_{90}$ (µg/mL) |
|---|---|---|---|
| CFDC | ≤0.031 to 1 | 0.063 | 0.5 |
| TMP/SMX | ≤0.031/≤0.589 to 16/304 | 0.125/2.375 | 0.25/4.75 |
| MINO | 0.063 to 4 | 0.25 | 1 |
| TGC | 0.125 to 8 | 1 | 2 |
| CPFX | 0.5 to >32 | 2 | 16 |
| CFPM | 2 to >32 | 32 | >32 |
| MEPM | 0.25 to >32 | >32 | >32 |
| CL | 0.125 to >32 | 4 | 16 |

***Conclusion.*** CFDC showed potent *in vitro* activity against *S. maltophilia*, including TMP/SMX-resistant isolates. CFDC also showed potent *in vivo* efficacy reflecting *in vitro* activity against *S. maltophilia* in murine systemic infection model.

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### 1367. Clinical Cure in Secondary Efficacy Populations in Patients With Complicated Urinary Tract Infection Treated With ZTI-01 (Fosfomycin for Injection): Findings From the ZEUS Trial

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***Background.*** ZTI-01 (fosfomycin for injection) is an investigational epoxide antibiotic with a differentiated mechanism of action (MOA) inhibiting an early step in bacterial cell wall synthesis. ZTI-01 has a broad spectrum of *in vitro* activity, including multidrug-resistant Gram-negative pathogens, and is being developed for the treatment of patients with complicated urinary tract infection (cUTI) and acute pyelonephritis (AP) in the United States.

***Methods.*** ZEUS was a multicenter, double-blind, Phase 2/3 trial in hospitalized adults with cUTI and AP to evaluate safety and efficacy. Randomized patients received 6 g ZTI-01 q8h or 4.5 g IV piperacillin/tazobactam (PIP-TAZ) q8h for 7 days; patients