Methods. 349 methicillin-sensitive and –resistant *S. aureus* (MSSA and MRSA, respectively) isolates were collected from various infection sources at multiple hospitals from 2015–2017 throughout the US, Greece, Hungary and Italy. In addition to the contemporary isolates, a set of 149 MSSA and MRSA clinical isolates from 2011 were also obtained from US hospital sources. MICs for CF-301 were determined using a new antimicrobial susceptibility testing (AST) medium for broth microdilution recently endorsed by Clinical and Laboratory Standards Institute (CLSI) for use with CF-301. The testing medium consists of cation-adjusted Muller Hinton Broth supplemented with 25% horse serum and 0.5 mM DTT (CAMHB-HSD). Susceptibility to conventional antibiotics was also examined in this study using standard methodology (CLSI document M07-A10) and included: vancomycin, trimethoprim-sulfamethoxazole, daptomycin, oxacillin, linezolid, clindamycin, and cefazolin.

Results. CF-301 had MIC_{50}, MIC_{90}, and MIC_{100} values of 0.5, 1, and 2 µg/mL, respectively, against each set of contemporary MSSA (n = 176) and MRSA (n = 173) clinical isolates. There were no differences noted with respect to the geographic source (in the US and Europe) of isolates. Furthermore, the CF-301 MICs reported here for 2015–2017 isolates were identical to that observed for MSSA and MRSA isolates from 2011.

Conclusion. CF-301 demonstrated potent in vitro activity against a total of 498 clinical *S. aureus* isolates from a range of human infections (including bacteremia) and different geographies. Contemporary clinical isolates did not demonstrate reduced susceptibility to CF-301 compared with the 2011 isolates.

Disclosures. **J. Oh**, ContraFect Corp: Employee, Salary; **R. Schuch**, ContraFect Corp: Employee, Salary

1214. Synergistic Antiviral Activity of S-033188/S-033447, a Novel Inhibitor of Influenza Virus Cap-Dependent Endonuclease, in Combination with Neuraminidase Inhibitors In Vitro

Mitsutaka Kitano, PhD[1]; Atsuko Yamamoto, MS[2]; Takeshi Noshi, MS[2]; Makoto Kawai, Ph. D.[2]; Ryu Yoshida, Ph. D.[2]; Akihiko Sato, Ph. D.[2]; Takao Shishido, Ph. D.[2] and Akira Naito, Ph. D.[2]; [1]SHIONOGI & CO., LTD.., Osaka, Japan, [2]SHIONOGI & CO., LTD., Toyonaka, Japan

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Background. S-033447, an active form of orally available prodrug S-033188, is a novel small molecule inhibitor of cap-dependent endonuclease that is essential for influenza virus transcription and replication. In this study, we evaluated the inhibitory effect of S-033188 in combination with neuraminidase inhibitors on the replication of influenza A/H1N1 virus in cultured cells.

Methods. The inhibitory effects of S-033447 in combination with NA inhibitors on the cytopathic effect of A/PR/8/34 strain in Madin–Darby canine kidney cells cultured for 2 days were tested and EC_{50} were determined. The combination index (CI), which were obtained when S-033188 and NA inhibitor were added at the closest ratio of each EC_{50} value, were used for the evaluation of these combinational effects (Table 1). CI values were calculated by the Chou and Talalay method, in which combinational effect were determined according to the criteria as follows: synergistic if CI ≤ 0.8, additive if 0.8 < CI < 1.2, and antagonistic if CI ≥ 1.2.

$CI = (D_{A/A+B})/D_A + (D_{B/A+B})/D_B + (D_{A/A+B} \times D_{B/A+B})/(D_A \times D_B)$

D_A: the EC_{50} of S-033447

D_B: the EC_{50} of NA inhibitor

$D_{A/A+B}$: the concentration of S-033447 giving 50% inhibition in combination with NA inhibitor at the closest ratio of each EC_{50} value

$D_{B/A+B}$: the concentration of NA inhibitor giving 50% inhibition in combination with S-033447 at the closest ratio of each EC_{50} value

Results. All CI values were lower than 0.8, under the condition that both S-033447 and NA inhibitor (oseltamivir acid, zanamivir hydrate, laninamivir, or peramivir trihydrate) were added at the closest ratio of each EC_{50} value (Table 1).

Conclusion. S-033447 in combination with oseltamivir acid, zanamivir hydrate, laninamivir, or peramivir trihydrate synergistically inhibited the replication of influenza A/H1N1 virus in MDCK cells.

Table 1. Combination effect of S-033447 and NA inhibitor in MDCK cells infected with A/PR/8/34 strain

Substance A	Substance B	D_A (nmol/L)	D_B (nmol/L)	$D_{A/A+B}$ (nmol/L)	$D_{B/A+B}$ (nmol/L)	CI	Combination effect
S-033447	oseltamivir acid	4.51	3171.97	1.17	586.94	0.49	synergistic
S-033447	zanamivir hydrate	4.49	1565.38	1.22	305.99	0.52	synergistic
S-033447	laninamivir	4.52	212.74	1.12	56.02	0.58	synergistic
S-033447	peramivir trihydrate	4.41	213.77	1.13	56.66	0.59	synergistic

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

1215. Activity of Tedizolid against Gram-Positive Clinical Isolates Causing Nosocomial- and Community-Acquired Infections in United States Hospitals (2014–2016)

Rodrigo E. Mendes, PhD; Dee Shortridge, PhD; S J Ryan Arends, PhD; Helio S. Sader, MD, PhD; Mariana Castanheira, PhD and Robert K. Flamm, PhD; JMI Laboratories, Inc., North Liberty, Iowa

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Background. Tedizolid (TZD) was approved for the treatment of acute bacterial skin and skin structure infections and is also under investigation for the treatment of hospital-acquired (HA) bacterial pneumonia. The activity of TZD and comparators were evaluated against gram-positive (GP) pathogens causing community (CA)-acquired and HA infections in the US.

Methods. During the Surveillance of Tedizolid Activity and Resistance (STAR) Program, 10,091 GP isolates were recovered from patients in 31 US hospitals. Isolates were identified by standard biochemical algorithms and MALDI-TOF MS. Susceptibility (S) testing followed CLSI methods and CLSI/EUCAST interpretation. CA and HA infections were defined based on CDC criteria.

Results. TZD ($MIC_{50/90}$, 0.12/0.12 µg/mL; 100.0%S) showed equivalent MIC_{50} and MIC_{90} values against MSSA and MRSA, regardless of infection type or origin of isolate (Table). Linezolid (LZD; $MIC_{50/90}$, 0.5–1/1 µg/mL; 100.0%S), daptomycin (DAP; $MIC_{50/90}$, 0.25/0.5 µg/mL; 99.5–100.0%S), vancomycin (VAN; $MIC_{50/90}$, 0.5–1/1 µg/mL; 100.0%S) and trimethoprim-sulfamethoxazole ($MIC_{50/90}$, ≤0.5/≤0.5 µg/mL; 93.0–99.5%S) were also active throughout against MSSA and MRSA, while MICs for other agents varied. TZD ($MIC_{50/90}$, 0.12/0.25 µg/mL; 100.0%S) activities were consistent against *E. faecalis* causing various infections from different origins, as were LZD ($MIC_{50/90}$, 1/1 µg/mL; 100.0%S), ampicillin ($MIC_{50/90}$, 1/1–2 µg/mL; 100.0%S), DAP ($MIC_{50/90}$, 1/1–2 µg/mL; 100.0%S), and VAN ($MIC_{50/90}$, 1/2 µg/mL; 94.9–97.0%S), although these agents had MIC_{50} and MIC_{90} values 4- to 8-fold higher than TZD. TZD ($MIC_{50/90}$, 0.12/0.25 µg/mL), LZD ($MIC_{50/90}$, 1/1–2 µg/mL; 97.6–100.0%S) and DAP ($MIC_{50/90}$, 1/2–4 µg/mL; 97.4–100.0%S) were active *in vitro* against *E. faecium*, regardless of infection type. *S. pneumoniae* isolates were S to several drugs tested, and ceftaroline showed the lowest MICs ($MIC_{50/90}$, ≤0.015/0.06 µg/mL; 100.0%S).

Conclusion. TZD had potent *in vitro* activity against GP isolates causing CA and HA infections in US hospitals, regardless of infection site or bacterial species. The TZD *in vitro* potency was also generally higher than clinically available comparator agents.

Organism[a]	Tedizolid MIC_{50}/MIC_{90} (µg/mL) for community- and hospital-acquired by infection site[b]		
	BSI	Pneumonia	SSSI
MSSA	0.12/0.12 – 0.12/0.12	0.12/0.12 – 0.12/0.12	0.12/0.12 – 0.12/0.12
MRSA	0.12/0.12 – 0.12/0.12	0.12/0.12 – 0.12/0.12	0.12/0.12 – 0.12/0.12
E. faecalis	0.12/0.25 – 0.12/0.25	NA – NA	0.12/0.25 – 0.12/0.25
E. faecium	0.12/0.25 – 0.12/0.25	NA – NA	0.12/0.25 – 0.12/0.25
S. pneumoniae	0.12/0.25 – NA	0.12/0.25 – NA	NA – NA

[a] MSSA, methicillin (oxacillin)-susceptible *S. aureus*; MRSA, methicillin (oxacillin)-resistant *S. aureus*.
[b] BSI, bloodstream infection; SSSI, skin and skin structure infection; NA, not available due to low number (<10 isolates) or absence of pathogen.

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1216. Antimicrobial Activity of Ceftolozane–Tazobactam Tested against Contemporary (2012–2016) *Enterobacteriaceae* and *Pseudomonas aeruginosa* Isolates by US Census Division

Dee Shortridge, PhD; Leonard R. Duncan, PhD; Michael A. Pfaller, MD and Robert K. Flamm, PhD; JMI Laboratories, Inc., North Liberty, Iowa

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Background. Ceftolozane-tazobactam (C-T) is a combination of a novel antipseudomonal cephalosporin and a well-described β-lactamase inhibitor. C-T was approved by the United States (US) Food and Drug Administration in 2014 for complicated urinary tract infections, including acute pyelonephritis and complicated intra-abdominal infections. C-T is currently in clinical trials for the treatment of nosocomial pneumonia. The Program to Assess Ceftolozane-Tazobactam Susceptibility (PACTS) monitors C-T resistance to gram-negative (GN) isolates worldwide. In this study, the activities of C-T and comparators vs. GN isolates from each of the 9 US Census divisions were compared.

Methods. A total of 18,856 *Enterobacteriaceae* (ENT) and 4,735 *Pseudomonas aeruginosa* (PSA) isolates were collected from 32 US hospitals in 2012–2016. Isolates were tested for susceptibility (S) to C-T and comparators by CLSI broth microdilution methodology in a central monitoring laboratory. Other antibiotics tested included amikacin (AMK), ceftazidime (CAZ), colistin (COL), meropenem (MER), and piperacillin-tazobactam (TZP). The following resistant phenotypes were analyzed for ENT: carbapenem resistant (CRE); extended-spectrum β-lactamase phenotype screen-positive (ESBL); and ESBL, nonCRE. or PSA, MER-nonsusceptible (NS), TZP-NS, and CAZ-NS isolates were analyzed. CLSI (2017) interpretive criteria were used.

Results. For all ENT, 94.2% were S to C-T, 91.5% were S to TZP, 98.0% were S to MER, and 98.8% were S to AMK; 1,697 (9.0%) were ESBL, nonCRE and 356 (1.9%) were CRE. For all PSA isolates, 97.4% were S to C-T, 99.3% were S to COL, 96.9% were S to AMK, and 81.2% were S to MER. The % C-T S for each division (DIV) are shown in the table. The % C-T S for ENT ranged from 98.1% (DIV 4) to 87.4% (DIV 2) and % C-T S for ESBL, nonCRE ranged from 93.8% in DIV 4 to 79.8% in DIV 7. For PSA, the % C-T S ranged from 99.6% in DIV 4 to 94.9% in DIV 9. Activity of C-T against PSA NS to MER, CAZ or TZP varied by division and was >80% for all except DIV 9.

Conclusion. Against PSA, only COL was more active than C-T. C-T demonstrated potent activity against PSA NS to other β-lactams. For ENT, overall activity was good. For both PSA and ENT, C-T varied by DIV.