Conclusion. This study confirmed the improved activity of ERV over TGC against *Bacteroides* and suggests that ERV may be an appropriate choice for infections involving these organisms.

Disclosures. **E. Goldstein**, Tetraphase Pharmaceuticals: Research Contractor, Research grant

1210. Broad *In Vitro* Activity Analysis of Tedizolid Compared with Other Agents against a Global Collection of Gram-Positive Isolates Causing Bloodstream Infections (2014–2016)

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Background. Tedizolid (TZD) is an oxazolidinone derivative with oral and intravenous formulations approved for the treatment of acute bacterial skin and skin structure infections in the US, European countries, and other regions. This study evaluated TZD's and comparators' activity against a collection of clinical isolates causing bloodstream infections (BSI).

Methods. A total of 7,284 gram-positive isolates collected during the Surveillance of Tedizolid Activity and Resistance (STAR) Program for 2014–2016 were included. Bacteria were identified by standard algorithms and MALDI-TOF-MS. Susceptibility (S) testing was performed by CLSI methods, and interpretation used CLSI and EUCAST criteria.

Results. This *Staphylococcus aureus* collection contained 33.8% methicillin-resistant isolates. TZD was the most potent agent tested against all *S. aureus* ($MIC_{50/90}$, 0.12/0.12 µg/mL; 100.0%S) and the MRSA subset (Table). Other tested agents described in Table also had *in vitro* MRSA coverage. 15.6% of enterococci were vancomycin-resistant, which were mostly *Enterococcus faecium* (59.8%). Linezolid (LZD), ampicillin, daptomycin (DAP), and vancomycin (VAN) showed equivalent MIC_{50} values (1 µg/mL) against *E. faecalis*, but these MIC_{50} results were 8-fold higher than TZD (MIC_{50}, 0.12 µg/mL). Although LZD and DAP were highly active (98.9–99.4%S) against *E. faecium*, TZD MICs were 8- to 16-fold lower that LZD and DAP. Ceftaroline (CPT) showed the lowest MIC values against *Streptococcus pneumoniae*, whereas TZD and VAN were similarly active. TZD and CPT showed the lowest MIC_{90} values against viridans group streptococci, while CPT, ceftriaxone, and penicillin had the lowest MIC_{90} results against β-hemolytic streptococci.

Conclusion. TZD had potent activities against this global population of gram-positive clinical isolates that caused BSI. This *in vitro* potency and a favorable pharmacodynamic profile may suggest TZD is a promising candidate for treating BSI caused by gram-positive isolates, especially *E. faecium*.

Organisms (no. tested)	MIC_{50}/MIC_{90} (µg/mL) and % susceptible for agents with oral formulations[a]				
	TZD	LZD	VAN	DAP	CPT
MRSA (1,365)	0.12/0.12/100.0	1/1/100.0	0.5/1/100.0	0.25/0.5/99.7	1/1/90.3
Enterococcus spp. (1,758)	0.12/0.25/-	1/2/99.5	1/>16/84.4	1/2/99.8	1/>8/68.6[c]
E. faecalis (1,089)	0.12/0.25/100.0	1/2/99.8	1/2/98.0	1/1/100.0	1/2/100.0[c]
E. faecium (620)	0.12/0.25/-	1/2/98.9	1/>16/59.8	2/2/99.4	>8/>8/11.1[c]
S. pneumoniae (373)	0.12/0.25/-	1/1/100.0	0.25/0.25/100.0	NA	≤0.015/0.12/100.0
VGS (388)	0.12/0.12/-	1/1/100.0	0.5/0.5/100.0	0.25/0.5/100.0	≤0.015/0.12/-
BHS (723)	0.12/0.25/-	1/1/100.0	0.25/0.5/100.0	0.12/0.25/100.0	≤0.015/≤0.015/100.0

[a] TZD, tedizolid; LZD, linezolid; VAN, vancomycin; DAP, daptomycin; CPT, ceftaroline. Susceptibility results displayed here were based on CLSI criteria.
[b] MRSA, methicillin-resistant *S. aureus*; VGS, viridans group streptococci; BHS, β-haemolytic streptococci.
[c] Represents ampicillin results.

Disclosures. **R. E. Mendes**, Merck: Research Contractor, Research grant; **D. Shortridge**, Merck: Research Contractor, Research grant; **H. S. Sader**, Merck: Research Contractor, Research grant; **L. R. Duncan**, Merck: Research Contractor, Research grant; **R. K. Flamm**, Merck: Research Contractor, Research grant

1211. *In vitro* Susceptibility Testing of Essential Oils against Gram-positive and Gram-negative Clinical Isolates, including Carbapenem-resistant *Enterobacteriaceae* (CRE)

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Background. In the era of antibiotic resistance, alternative anti-infectives must be explored. The National Action Plan for Combating Antibiotic-Resistant Bacteria calls for developing nontraditional therapeutics, including natural compounds such as essential oils (EOs) (Goal 4.4). A pilot study previously showed *in vitro* activity of EOs against CRE and warranted further study of their antibacterial activity. We studied cinnamon bark, clove, lavender, lemongrass, eucalyptus, oregano, rosemary, thyme, tea tree, manuka, and Thieves® blend (Young Living Essential Oils, Lehi UT) against an expanded panel of Gram-positive and Gram-negative isolates.

Methods. 30 Gram-positive and 70 Gram-negative clinical isolates, including CRE, were tested using CLSI methods. Isolates were grown overnight on TSA; 0.5 McFarland suspensions in sterile water were swabbed over Mueller–Hinton agar using the Kirby–Bauer method. 20 µl of full-strength oils were pipetted onto blank paper disks in a sterile dish. Disks were placed aseptically onto the plates immediately after inoculating disks. Vancomycin was tested with Gram-positives and meropenem with Gram-negatives. Median zone diameters are shown.

Results. EOs oregano, thyme, cinnamon bark, and lemongrass had the largest zones of inhibition against Gram-positive organisms and were larger than those of vancomycin for MRSA/MSSA. Cinnamon bark had the largest zone of inhibition against *P. aeruginosa* and was larger than that of meropenem. Oregano, thyme, cinnamon bark had the largest zones of inhibition against *Enterobacteriaceae* and were larger than those of meropenem against *K. pneumoniae* and *E. cloacae*.

Table 1. Median Zone Diameters (mm for Essential Oils)

Isolates	Oregano	Thyme	Cinnamon Bark	Lemongrass	Manuka	Clove	Tea Tree	Thieves®	Vanco	Mero
MRSA *n* = 10	23	26	30	30	13	13	9	18	18	ND
MSSA *n* = 10	26	30	29	30	18	15	8.5	19	19	ND
S. pyogenes n = 10	18	19.5	13	22	14	13	6.5	18.5	20.5	ND
E. coli n = 20	21.5	20	24	ND	6	12	13	13	ND	30
K. pneumoniae n = 20	20	15	22	ND	6	11.5	15	12	ND	13
Ps. aeruginosa n = 15	6	6	17	ND	6	6	6	8	ND	7
E. cloacae n = 15	20	16	21	ND	6	10	15	11	ND	25.5

ND=not done

Conclusion. Essential oils showed significant *in vitro* activity against clinical isolates, including CRE. Further study of the clinical activity of essential oils is warranted.

Disclosures. **J. E. Patterson**, Young Living Essential Oils: Independent Contractor, Salary

1212. Lysin CF-301 Demonstrates In Vitro Synergy with Conventional Antibiotics against *Staphylococcus aureus*

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Background. CF-301 is a novel, recombinantly-produced bacteriophage-derived lysin (cell wall hydrolase) and is the first agent of this class to enter clinical development in the US for the treatment of bacteremia including endocarditis due to *S.aureus*. This study evaluated the in vitro activity of CF-301 combined with each of 7 antistaphylococcal antibiotics including those considered to be current standard of care treatments for *S.aureus* bacteremia (daptomycin, vancomycin, oxacillin, nafcillin, and cefazolin) as well as linezolid and telavancin.

Methods. MICs for CF-301 were determined using a new AST medium for broth microdilution recently endorsed by the CLSI for use with CF-301. The testing medium consisted of cation-adjusted MHB supplemented with 25% horse serum and 0.5 mM DTT. Synergy was determined by checkerboard microdilution using the fractional inhibitory concentration index (FICI) for each combination in triplicate. For each antibiotic tested, an FIC mean was derived from each set of checkerboards by averaging 3 consecutive FIC values along the growth/no growth interface for each plate. Thus, 9 values were, used to generate the final mean. Synergy was defined as an FICI of ≤0.5; indifference was >0.5 to <2; and antagonism was ≥2. Each combination was examined against 10 MSSA and 10 MRSA strains.

Results. CF-301 synergized with daptomycin and vancomycin against each MSSA and MRSA strain, with FICI values between 0.254 and 0.5. Synergy was similarly observed against all 20 strains tested with oxacillin and nafcillin (FICI = 0.25–0.5); for the third β-lactam, cefazolin, synergy was observed with 17 strains (FICI = 0.75, for the remaining 3 strains). CF-301 synergized with televancin against 70% of the strains (FICI = 0.375–0.5), and was indifferent with the remainder (FICI = 0.625–1). CF-301 synergized with linezolid against 55% of the strains (FICI = 0.375–0.5), and was indifferent with the remainder (FICI = 0.625–0.75).

Conclusion. The broadly synergistic activity of CF-301 with conventional antistaphylococcal antibiotics against MSSA and MRSA suggests that CF-301 may afford therapeutic benefit by potentiating the activity antibiotics to treat serious infections for which there is an unmet medical need to improve outcomes.

Disclosures. **K. Sauve**, ContraFect Corp: Employee, Salary; **A. Jandourek**, ContraFect Corp: Employee, Salary; **C. Cassino**, ContraFect Corp: Employee, Salary; **R. Schuch**, ContraFect Corp: Employee, Salary

1213. Activity of Antistaphylococcal Lysin CF-301 against Contemporary *Staphylococcus aureus* Clinical Isolates from the USA and Europe

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Background. CF-301 is a novel, recombinantly-produced bacteriophage-derived lysin (cell wall hydrolase) and is the first agent of this class in the US to enter into clinical development for the treatment of bacteremia including endocarditis due to *S. aureus*. Hallmark features of CF-301 include rapid and pathogen-specific bacteriolytic activity, synergy with antibiotics, biofilm-disrupting activity, a low propensity for resistance, and the capacity to suppress antibiotic resistance. This is the first report of an international surveillance study for CF-301.

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

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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)

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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

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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.