bacteremia (80%, 52/65). Bacteremia was cleared in 90.8% (59/65) of patients and the 30-day mortality rate was 15.4% (10/65). Median time to bacteremia clearance after combination switch was 3 days. Eleven patients received DAP-CPT within 72 hours of index culture. Median time to bacteremia clearance for patients switched to DAP-CPT within 72 hours versus after 72 hours did not differ (2 vs 3 days; P = 0.526), however the overall median duration of bacteremia was 4 and 11 days (P = 0.018). In a sub analysis, the median time of bacteremia clearance following combination therapy was significantly longer for patients receiving renal replacement therapy (5 vs 2 days; P = 0.04).

Conclusion. There were no independent predictors of 30-day mortality identified. DAP-CPT combination therapy resulted in clearance of persistent bacteremia and may serve as an effective salvage therapy.

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1625. Real-World Outpatient Utilization of Ceftolozane/Tazobactam in Physician Office Infusion Centers (OICs)

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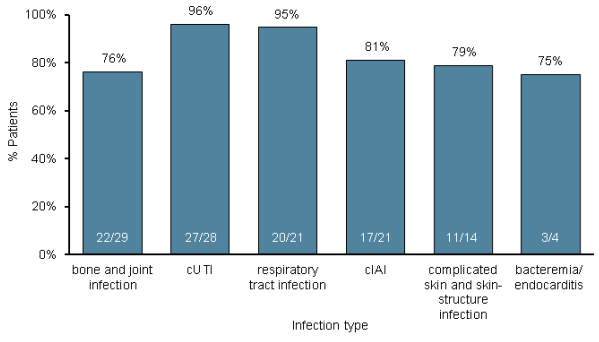
Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Ceftolozane/tazobactam (C/T) is indicated for the treatment (tx) of complicated Gram-negative infections including urinary tract infection (cUTI), intra-abdominal infection (cIAI), and hospital-acquired/ventilator-associated bacterial pneumonias caused by susceptible bacteria. Real-world data on the use of C/T are limited. We present a multicenter observational review of C/T outpatient utilization in Infectious Disease OICs.

Methods. Medical records of patients (pts) who received C/T for ≥3 doses from May 2015 to Sept 2019 were reviewed. Data included demographics, diagnosis, disease history, pathogens, C/T tx hospitalizations, emergency department (ED) visits and clinical outcomes. Clinical success was defined as complete or partial symptom resolution at completion of C/T with oral antibiotics as needed. Persistent infection and early discontinuation (D/C) of C/T were deemed non-successful. Indeterminant outcomes were deemed non-evaluable. Chi Square, Fisher's exact, and t-tests were used to identify characteristics associated with clinical outcome.

Results. 120 pts (mean age: 59±15 years, 60% male) from 33 OICs were identified. Median Charlson score was 5 (IQR, 3-7), with 43% immunocompromised, and 77% refractory/recurrent disease. Primary infections were bone and joint (25%), cUTI, (24%), respiratory tract (18%), cIAI (18%), complicated skin and skin-structure (12%), and bacteremia/endocarditis (3%). Most pts had multi-drug resistant Gram-negative pathogens (80/108; 74%), predominantly *Pseudomonas aeruginosa*. Polymicrobial infections were reported in 44%. Median duration of C/T therapy was 21 days (IQR, 14-34). C/T was initiated in the OIC in 59% of pts. Overall clinical success was 86% (100/117), with rates by infection type in Fig 1. Non-success was reported in 17, 10 due to persistent infection and 7 due to adverse events. The adverse events led to early D/C of C/T, all with resolution. Statistically, infection type did not impact success rate. Hospitalizations and ED visits during tx occurred in 5% of pts with successful outcomes and 35% of pts with non-successful outcomes ($p < 0.001$).

Fig 1. Clinical success rates of C/T by infection type



Conclusion: These real-world results support the effectiveness of C/T in a wide variety of complicated Gram-negative infections treated in the outpatient setting.

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1626. Synergistic Effect of Cefiderocol with Other Antibiotics Against PER-Producing *Acinetobacter baumannii* Isolates from the Multinational SIDERO-WT Studies

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Cefiderocol (CFDC), a novel siderophore cephalosporin, showed potent activity at minimum inhibitory concentrations (MICs) of ≤4 μg/mL against ≥99% of Gram-negative isolates in the multinational SIDERO-WT studies. PER-producing *Acinetobacter baumannii,* mainly from Russia, showed high CFDC MICs of 8– >64 μg/mL. This study evaluated the synergistic effects of CFDC combined with other antibiotics against PER-producing *A. baumannii* isolates with high CFDC MICs.

Methods. Two isolates of PER-producing *A. baumannii* with resistance to CFDC (MIC 16 μg/mL), meropenem (MEM; MIC 64 μg/mL), ceftazidime-avibactam (CZA; MIC 64/4 μg/mL), amikacin (AMK; MIC 32 or 64 μg/mL), and ciprofloxacin (CIP; MIC ≥64 μg/mL) were tested. Against ampicillin-sulbactam (SAM), one isolate was resistant (MIC 32/64 μg/mL) and another was susceptible (MIC 8/16 μg/mL). Effects of CFDC combined with other antibiotics were evaluated by checkerboard assay and chemostat model reproducing humanized antibiotic exposure. The checkerboard assay used a single agent (e.g. ceftazidime [CAZ], avibactam [AVI], ampicillin [AMP] or sulbactam [SUL]). Iron-depleted cation-adjusted Mueller–Hinton broth was used as the standard medium for CFDC, as recommended by the Clinical Laboratory and Standards Institute.

Results. Against both isolates, synergy with CFDC was seen for two β-lactamase inhibitors, AVI and SUL, with a fractional inhibitory concentration (FIC) index of 0.026–0.033 and 0.26–0.27, respectively. A synergistic to additive effect was seen for MEM and AMK, with an FIC index of 0.53–0.75 and 0.25–0.52, respectively. In the chemostat model, regrowth during 24-h treatment was observed with single agents (CFDC 2 g, q8h, 3-h infusion; MEM 2 g, q8h, 1-h infusion; CZA 2 g, q8h, 2-h infusion; SAM 3 g, q8h, 3-h infusion; AMK 15 mg/kg, q8h, 3-h infusion) for both isolates, including the SAM-susceptible isolate. However, no regrowth was seen when CFDC was combined with CZA, MEM, SAM or AMK.

Conclusion. The most potent synergy was seen between CFDC and AVI against PER-producing *A. baumannii* with a decreased MIC to ≤1 μg/mL for all isolates, followed by SUL and MEM. Under humanized pharmacokinetic exposure, combination of CFDC and CZA, MEM, SAM or AMK is expected to be effective against PER-producing *A. baumannii* in spite of high CFDC MICs.

Disclosures. Yoshinori Yamano, PhD, Shionogi & Co., Ltd. (Employee) Miki Takemura, MSc, Shionogi & Co., Ltd. (Employee) Naomi Anan, MSc, Shionogi & Co., Ltd. (Employee) Rio Nakamura, BSc, Shionogi & Co., Ltd. (Employee) Roger Echols, MD, Shionogi Inc. (Consultant)

1627. Tedizolid is Well-tolerated Among Patients Receiving Prolonged Treatment Courses, Including Those Who are Intolerant of Alternative Agents

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Tedizolid (TZD) is approved for acute bacterial skin and skin structure infections (ABSSSI), but often used for complicated infections to avoid linezolid (LZD) adverse events (AE), particularly when long-term treatment is indicated. This studied aimed to characterize the tolerability of TZD, including patients (pts) receiving prolonged treatment.

Methods. Retrospective review of pts who received TZD > 72 hours. Thrombocytopenia was defined as a 50% decrease from baseline platelet count. Favorable clinical outcome was defined as completing therapy without an AE or hospital readmission within 30 days.

Results. 86 pts accounting for 102 courses were included. Median age of pts was 57 years and 43% were immunocompromised. Median duration of TZD therapy was 8 days (range: 4 – 350) and 32% of courses were >14 days. Common indications were ABSSSI (n=42), bacteremia (n=15), intra-abdominal infection (n=11), and pneumonia (n=10). 47% and 5% of courses were associated with MRSA or VRE and M. abscessus, respectively. 44% of TZD courses were preceded by treatment failure or AE associated with alternative therapies. AEs attributed to LZD were documented in 13 patients: thrombocytopenia (n=11), lactic acidosis (n=1), or both (n=1). Serotonergic agents were administered during 76% of TZD courses; however, no patient developed serotonin syndrome. 8% of TZD courses were stopped prematurely due to AEs that included thrombocytopenia (n=3), gastrointestinal intolerance (n=2), confusion (n=1), eosinophilia (n=1) and thrombocytopenia with lactic acidosis (n=1). All cases of thrombocytopenia occurred in pts with baseline platelets < 100,000 cells/L. 79% of pts receiving > 14 days of TZD completed therapy successfully without AEs. Among pts who failed alternative therapies, 74% were able to tolerate TZD and completed therapy. Overall, 80% of courses were completed with a favorable outcome.

Clinical Outcomes of Extended TZD Therapy

Clinical Outcomes	Unique Courses of TZD N = 102
Favorable Outcome (No ADRs requiring discontinuation + clinical cure)	82 (80.4%)
Adverse events requiring discontinuation	8 (8.0%)
Thrombocytopenia	3
GI intolerance	2[a]
Confusion	1[b]
Eosinophilia	1[b]
Thrombocytopenia + lactic acidosis	1
In hospital death/transfer to hospice	5 (4.9%)
Failed therapy/readmission	2 (2.0%)
Ongoing Suppression	1 (1.0%)[c]
Thrombocytopenia	
>50% decrease during treatment course	11 (10.8%)
Total platelets < 50K (Baseline platelet range 16 – 86)	11 (10.8%)
>50% decreased AND total platelets <50K ▪ 83K →40K ▪ 16K →5K ▪ 86K →26K	3 (2.9%)
Baseline Platelets > 100K with >50% decrease	8/85 (9.4%)
Baseline Platelets < 100K with >50% decrease	3/17 (17.6%)

[a] Both cases were the same patient who subsequently tolerated 31 day treatment course
[b] Persisted after TZD discontinuation and later determined to be unrelated to TZD
[c] >350+ days

Conclusion. The safety of prolonged TZD treatment is not well-described. In our experience, TZD was well-tolerated, including among pts who failed alternative therapy. No pt receiving concomitant serotonergic agents developed serotonin syndrome and thrombocytopenia occurred exclusively among pts with low baseline platelets. Treatment courses >14 days were not associated with an increase in the rate of AEs.

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1628. Treatment Heterogeneity in *Pseudomonas aeruginosa* Pneumonia

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Serious bacterial infections present a unique challenge for studies of real-world evidence. Often, the causative organism is unknown during the initial period of treatment and clinical symptoms change day-to-day, which lead to multiple changes in therapy. While it is assumed approaches to treating specific infectious diseases are mostly similar, we've previously identified substantial treatment heterogeneity, even among organism-specific and site-specific infections.

Methods. Our retrospective cohort study included inpatients with positive *P. aeruginosa* from sputum and bronchoalveolar lavage cultures collected during VA medical center and community living center stays from 01/15-04/18. We included the first positive culture during the admission per patient. Daily antibiotic exposures were mapped from 3 days prior to the culture collection date until discharge or 30 days for longer stays. Heterogeneity was defined as patterns of antibiotic treatment (drug and duration) not shared by any other patient.

Results. Our study included 5,435 patients and 87.4% of patients had different patterns of antibiotic drug and duration. Among patients with changes in therapy (84.0%), 96.9% had different antibiotic treatment patterns, with a median time to first change of 1 day and median of 3 changes. When restricting the analysis to antibiotic classes (rather than drug), Gram-negative antibiotics, and anti-pseudomonal antibiotic classes, heterogeneity was 81.8%, 52.0%, and 48.7%, with median time to first change of 1, 3, and 3 days, and a median of 3, 2, and 2 changes, respectively.

Conclusion. Among inpatients with positive *P. aeruginosa* respiratory cultures, substantial heterogeneity was observed in the national VA Healthcare System. Even at the class level, and restricting the analysis to anti-pseudomonal antibiotic classes, approximately 50% of patients had different treatment patterns during their inpatient stay. Current methods to assess treatment do not adequately account for the extensive heterogeneity observed in infectious diseases and it remains unclear how local or national treatment guidelines affect heterogeneity.

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1629. Vancomycin Resistance in *Enterococcus faecium* Clinical Isolates Responsible for Bloodstream Infections in US Hospitals Over Ten Years (2010-2019) and Activity of Oritavancin

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. *Enterococcus faecium* (EFM) causes difficult-to-treat infections due to its intrinsic resistance (R) and ability to acquire R to many antimicrobials. This study evaluated the vancomycin (VAN)-R rates over time and the activity of oritavancin (ORI) against a collection of EFM causing bloodstream infections (BSI).

Methods. A total of 1,081 BSI EFM isolates collected from 36 US hospitals in a prevalence mode design during 2010-2019 were evaluated. Bacterial identification was confirmed by MALDI-TOF MS. Susceptibility testing was performed by reference broth microdilution. For comparison, the ORI breakpoint for VAN-susceptible *E. faecalis* was applied to EFM. Isolates were characterized as VanA or VanB phenotypes based on their susceptibility (S) to VAN and teicoplanin (TEC). The VanB phenotype was confirmed by PCR and/or whole genome sequencing.

Results. Overall, 72.3% (782/1,081) of EFM were VAN-R (Table). VanA was the most common phenotype (97.7%; 764/782). The yearly VAN-R rates decreased from 81.8% in 2010 to 58.7% in 2019. A total of 18 (2.3%) isolates exhibited a VanB phenotype (TEC MIC, 0.5-8 mg/L); however, the *vanB* gene only was confirmed in 9 EFM isolates (TEC MIC, 0.5-1 mg/L), which were all collected in 2010-2012. The remaining 9 (50.0%) VanB phenotype EFM isolates carried a *vanA* gene (TEC MIC, 4-8 mg/L). ORI was very active against VAN-susceptible EFM ($MIC_{50/90}$, ≤ 0.008/≤0.008/mg/L), VanA ($MIC_{50/90}$, 0.03/0.12 mg/L; MIC_{100}, 0.5 mg/L), and VanB ($MIC_{50/90}$, ≤ 0.008/0.015 mg/L; MIC_{100}, 0.03 mg/L) subsets. Only linezolid (LZD) and ORI (MIC, ≤ 0.12 mg/L) showed > 95.0%S against EFM and VAN-R subsets. Daptomycin (DAP)-R rarely was observed (0.8%), but it was more frequently found in the last 5 years. However, 49.9% of EFM isolates showed elevated DAP MICs (2 and 4 mg/L). ORI inhibited 77.8%, and 100.0% of DAP-R and LZD-nonsusceptible EFM isolates at ≤ 0.12 mg/L, respectively.

Conclusion. VAN-R rates among EFM causing BSI in the US decreased during 2010-2019. VanA remains the most common phenotype, whereas *vanB*-carrying isolates became rarer in later years. Interestingly, half of VanB-phenotype isolates carried a *vanA* gene. ORI was very active against EFM causing BSI, including isolates R to VAN, DAP, and/or nonsusceptible to LZD.

Table 1

Organism / resistant subset (n)	Occurrence (%) per study year											Oritavancin $MIC_{50/90}$ (mg/L)
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	All years	
E. faecium (1,081)	269*	138*	76*	70*	74*	90*	92*	90*	90*	92*	108**	
Oritavancin $MIC_{50/90}$ (mg/L)	0.03/0.06	0.03/0.12	0.03/0.12	0.03/0.06	0.015/0.06	0.03/0.12	0.015/0.03	0.015/0.06	0.015/0.06	0.015/0.06	0.03/0.06	
Vancomycin-R (782)	81.8	74.6	78.9	75.7	68.9	66.7	65.2	67.8	66.7	58.7	72.3	0.03/0.12
VanA phenotype (764)	79.6	72.5	77.6	75.7	64.9	65.6	65.2	66.7	64.4	57.6	70.7	0.03/0.12
VanB phenotype (18)	2.2	2.2	1.3	0.0	4.1	1.1	0.0	1.1	2.2	1.1	1.7	≤0.008/0.015
vanB genotype (9)	1.9	1.4	1.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.8	≤0.008/-
Daptomycin-R (9)	0.0	1.4	0.0	0.0	0.0	2.2	2.2	0.0	0.0	3.3	0.8	0.015/-
Daptomycin MIC, 2-4 mg/L (S40)	63.9	59.4	64.5	55.7	71.6	28.9	43.5	23.3	35.6	28.3	50.0	0.03/0.12
Linezolid-NS (13)	2.2	0.7	0.0	1.4	1.4	0.0	2.2	0.0	2.2	0.0	1.2	0.015/0.06
Ampicillin-R (944)	93.3	91.3	90.8	90.0	91.9	83.3	77.2	85.6	81.1	77.2	87.3	0.03/0.12

* Number of *E. faecium* isolates
R, resistant; NS, nonsusceptible

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