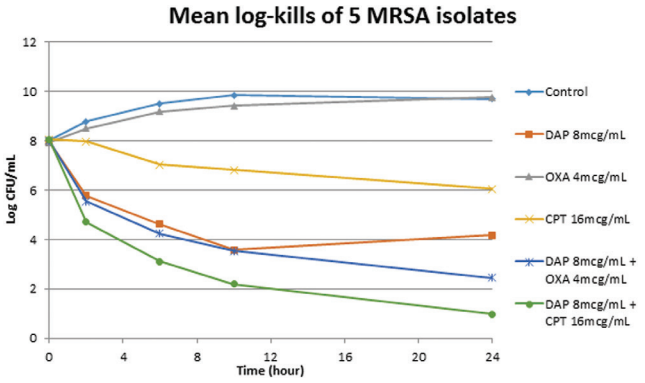
CFU/mL) against 60% and 20% of isolates exposed to DAP+CPT or DAP+OXA, respectively.

Conclusion. Among persistent MRSA bloodstream isolates, combinations of DAP + CPT or OXA demonstrates synergy and statistically greater killing effects *in vitro* at fCmax concentrations than DAP alone. Log-kills were greatest with DAP+CPT, which merits further validation in pre-clinical models.



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

2404. Telavancin (TLV) and Vancomycin (VAN) Activity and Impact on Mechanical Properties When Incorporated into Orthopedic Bone Cement

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Background. To increase available antibiotics for local administration in total joint replacements, this study investigated TLV and VAN added to Palacos® bone cement. Mechanical properties and antimicrobial activity of eluted antibiotics on common causative orthopedic implant pathogens were assessed.

Methods. Palacos (40 g package) samples were loaded with TLV or VAN powder (control 2.0 g) to test drug activity and mechanical properties: bending, compression, and fracture toughness. Samples were prepared following clinical standards and as previously described (Slane *et al.*, 2014 MSE 42: 168–176). All mechanical samples were wet cured for 21 days in PBS at 21°C before testing in accordance with ISO 5833. With a starting inoculum of 10^3 CFU/mL, antibiotic activity was measured for 14 days against: two methicillin-resistant *S. aureus*, one methicillin-susceptible *S. aureus* and one *S. epidermidis*.

Results. The eluted dosages from samples with 0.25 g VAN or more per Palacos package were sufficient to eliminate a 10^3 CFU/mL inoculum of *S. aureus* organisms. 2.0 g of TLV was required to achieve the same bactericidal effect. TLV 2.0 g was able to fully clear the initial inoculum of a high biofilm producing *S. epidermidis*. No tested vancomycin dosage replicated these results. Adding more than 0.5 g of TLV or VAN per Palacos package reduced compressive yield strength to (VAN) or below (TLV) the ISO 70MPa minimum. Fracture toughness and flexural strength were not significantly altered with either antibiotic.

Conclusion. Adding either TLV or VAN to Palacos before polymerization reduced bending properties similarly but maintained ISO standards. More VAN than TLV can be added and still maintain compressive yield strength above ISO requirements (1.0 g VAN vs. 0.5 g TLV). VAN eliminated the tested *S. aureus* strains at a lower added mass. However, TLV was more effective against a high biofilm producing *S. epidermidis*. VAN was highly effective at eliminating a bacterial inoculum consistent with surgical contamination while maintaining ISO standards. The authors would like to acknowledge Theravance Biopharma US, Inc. for their support and funding.

Disclosures. **A. Bishop**, Theravance: Investigator, Educational support, Research support and Salary. **S. Kim**, Theravance: Investigator, Research grant and Research support. **W. Rose**, Theravance: Consultant and Grant Investigator, Consulting fee and Research grant.

2405. *In vitro* Synergistic Activity of Sitafloxacin in Combination With Colistin Against Clinical Isolates of Multidrug-Resistant *Acinetobacter baumannii* in Thailand

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Background. Multidrug-resistant *Acinetobacter baumannii* (MDR-AB) is a major cause of nosocomial infections, and associated with high mortality rate. The objective of this study was to test synergistic effect of sitafloxacin and colistin against MDR-AB clinical isolates in Thailand.

Methods. The synergistic effect of sitafloxacin in combination with colistin against the 264 MDR-AB clinical isolates from 13 tertiary care hospitals in Thailand were tested. The fractional inhibitory concentration index (FICI) of combination was determined using the checkerboard method according to CLSI 2016. Time–kill assays were performed for 2 strains (H25 and K21) using sitafloxacin alone and in combination with colistin.

Results. The MICs of sitafloxacin and colistin range from 0.0156 to 8 µg/mL, and 0.5–16 µg/mL, respectively. The results of synergy testing for the 264 MDR-AB isolates are shown in Table 1. Sitafloxacin reduced the MIC of colistin 2-fold to 8-fold from the original concentrations (Figure 1). From 43 colistin-resistant isolates in combination tested, 39 isolates (90.7%) become susceptible to colistin. In the time-kill assay, synergistic effects were found for two isolates in all concentrations tested, and bactericidal activity was observed within 4 hours and maintained over 24 hours (Figures 2 and 3).

Conclusion. The synergistic effect of sitafloxacin and colistin combination was found. Most of isolates had at least a 2-fold decrease in MIC of colistin, which could be implied to reduce dose of colistin 50% from regular dose. Sitafloxacin combined with colistin may be benefit for alternative treatment of MDR-AB infections.

Table 1: Synergistic Effect of Sitafloxacin and Colistin Against MDR-AB Isolates (*n* = 264) Using the Checkerboard Assay

	No. of Isolates (%)				
Antimicrobial Agents	Synergy (FICI ≤0.5)	Partial Synergy (FICI >0.5–<1)	Additive (FICI = 1)	Indifference (FICI >1–<4)	Antagonism (FICI ≥4)
Sitafloxacin and colistin	9(3.4)	99(37.5)	75(28.4)	81(30.7)	0(0)

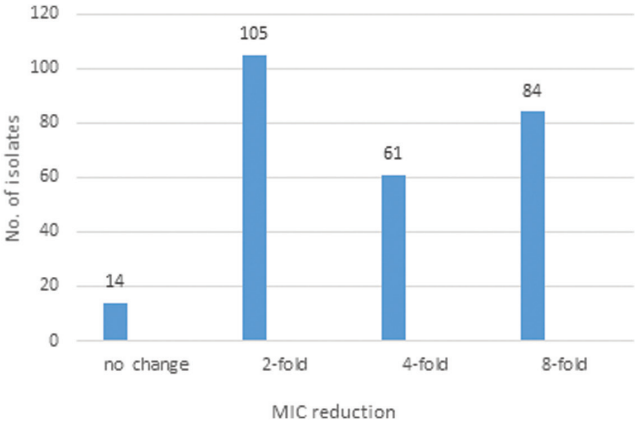

Figure 1: MIC reduction of colistin in combination with sitafloxacin against MDR-AB (*n* = 264).

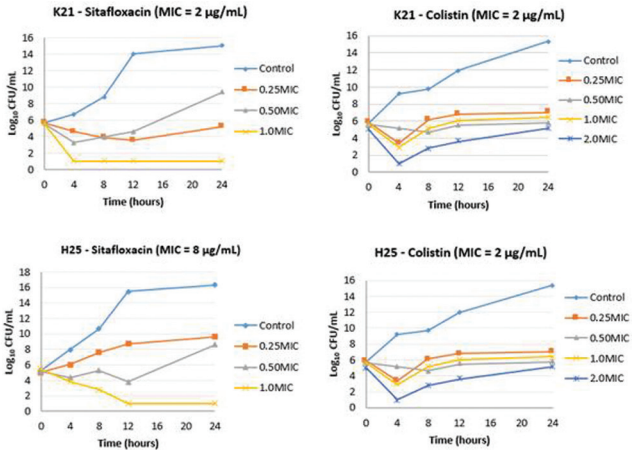

Figure 2: Time–kill curves for sitafloxacin and colistin alone against two isolates of MDR-AB.

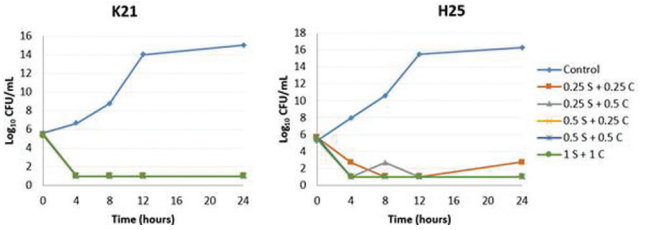

Figure 3: Time–kill curves with various concentrations of colistin (C) and sitafloxacin (S) in combination against two isolates of MDR-AB.

Disclosures. **T. Paiboonvong**, Daiichi Sankyo (Thailand) Ltd.: Grant support, Research support. **P. Montakantikul**, Daiichi Sankyo (Thailand) Ltd.: Grant support, Research grant.

2406. "Real-world" Treatment of Multidrug-Resistant (MDR) or Extensively Drug-Resistant (XDR) *P. aeruginosa* Infections With Ceftolozane/Tazobactam (C/T) vs. a Polymyxin or Aminoglycoside (Poly/AG)-based Regimen: A Multicenter Comparative Effectiveness Study

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Background. The emergence of MDR/XDR *P. aeruginosa* has led to a reliance on suboptimal agents (Poly/AG) for the management of infections due to this pathogen. C/T is a novel agent with excellent *in vitro* activity against resistant *P. aeruginosa* that is indicated for cUTI and cIAI and being reviewed for VABP; however real-world comparative data for invasive infections are lacking. The purpose of this study was to assess comparative rates of clinical cure, mortality, and acute kidney injury (AKI) among patients treated with C/T vs. a Poly/AG based regimen for *P. aeruginosa* infections

Methods. This was a retrospective, multi-site cohort of adult inpatients from January 1, 2012 to February 28, 2018 with infections due to MDR or XDR *P. aeruginosa*. Patients treated for ≥48 hours with C/T or a Poly/AG-based regimen were eligible for inclusion. Patients with a creatinine clearance <20 mL/minute, or those requiring renal replacement therapy at baseline were excluded. Bivariate comparisons for baseline clinical characteristics and outcomes were assessed.

Results. A total of 117 (57 C/T, 60 Poly/AG) patients were included. Baseline characteristics, infection source, severity of illness, and time to appropriate therapy were similar between the treatment groups. Mean age was 58.6 ± 15.1 years, and 70% were male. Common comorbidities included diabetes (35%) and CHF (28%), and the median (IQR) Charlson Comorbidity Index was 3 (1–4). 42% of the population presented with severe sepsis or septic shock, and 68% were in the ICU at the onset of the infection. The most common infections were ventilator associated (54%) or hospital acquired (17%) pneumonia. Combination therapy was more frequently used in the Poly/AG group (72% vs. 12%; $P < 0.001$) Treatment with C/T was associated with a higher rate of clinical cure (79% vs. 62%; $P = 0.046$) and a lower incidence of AKI (7% vs. 33%; $P < 0.001$) compared with Poly/AG based therapy. In hospital mortality rates were similar (28% vs. 37%; $P = 0.33$). No patients receiving C/T had hypersensitivity reactions, neurological adverse events, or *C. difficile* infections.

Conclusion. This multi-center retrospective analysis provides real-world data supporting improved outcomes with C/T compared with Poly/AG based regimens for invasive infections due to MDR/XDR *P. aeruginosa*.

Disclosures. **J. M. Pogue**, Merck: Consultant, Grant Investigator and Speaker's Bureau, Consulting fee, Grant recipient and Speaker honorarium. Allergan: Speaker's Bureau, Speaker honorarium. **K. S. Kaye**, Merck: Consultant and Grant Investigator, Consulting fee and Research grant. **A. Ray**, Merck: Speaker's Bureau, Speaker honorarium. **L. Puzniak**, Merck: Employee, Salary. **F. Perez**, Merck: Grant Investigator, Grant recipient.

2407. Emerging Piperacillin/Tazobactam Resistance in *Escherichia coli* and *Klebsiella* sp.

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Background. Piperacillin / tazobactam (P/T) plays an important role in the empirical therapy of many infections. While *Enterobacteraciae* resistance to P/T remains relatively low in our institution we have identified an increasing number of *E. coli* and *Klebsiella* sp. isolates with intermediate susceptibility or resistance to P/T (P/T-R). We report the increasing prevalence of P/T-R among *E. coli* and *Klebsiella* sp., antimicrobial usage, and attempts to document the mechanism of resistance in these isolates.

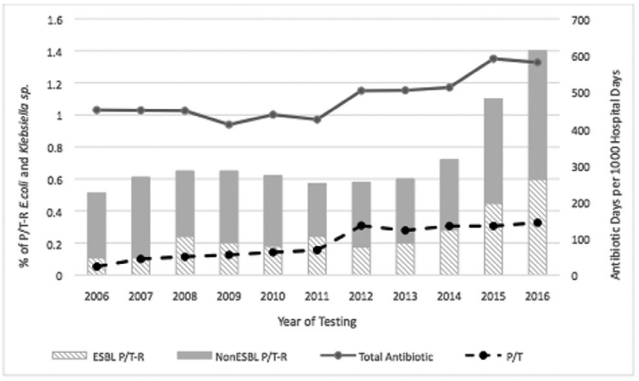
Methods. Antimicrobial susceptibility results using Kirby Bauer disk diffusion method for *E. coli* and *Klebsiella* sp. from all clinical sites (hospitalized patients) were reviewed from January 2006 through December 2016. Duplicates were excluded. Antimicrobial use was expressed as the number of hospital days on antimicrobials per 1000 hospital days. Whole genome sequencing was performed on a subset of isolates identified as P/T-R in order to identify a mechanism of resistance.

Results. From 2006 through 2016 we identified 126,422 *E. coli* and *Klebsiella* sp. isolates; 978 were P/T-R (0.78%). Of these 336 were extended spectrum β lactamase (ESBL) producers. Of the 642 non ESBL- P/T-R, 179 (27.8%) retained susceptibility to all cephalosporins tested. Figure 1 shows the distribution of P/T-R isolates and total antibiotic and P/T use in hospitalized patients. Whole genome sequencing of 4 isolates (*K. pneumoniae* from blood; $n = 3$ and *E. coli* from urine; $n = 1$) showed the presence of Class A β-lactamase genes; SHV ($n = 3$) and TEM ($n = 1$). All isolates showed the presence genes for outer membrane porins and protein efflux pumps; however, there were no detectable mutations that could explain the phenotypic susceptibility profile seen in these isolates.

Conclusion. We describe a novel phenotypic resistance pattern to P/T in *E. coli* and *Klebsiella* sp. which doubled in incidence from 2013 to 2016. This is concurrent with increasing P/T and overall antimicrobial use during the same time period. While a porin mutation has been described in similar strains, we have not been able to demonstrate this mechanism of resistance to date. Clinicians should be aware of this emerging resistance pattern when prescribing empiric antimicrobials.

Figure 1.

Figure 1.



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

2408. Delayed Appropriate Antimicrobial Therapy Does Not Affect the Clinical Outcome of Patients With Acute Pyelonephritis by Extended-Spectrum β-Lactamase-Producing *Enterobacteriaceae*

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Background. Extended spectrum β-lactamase-producing *Enterobacteriaceae* (ESBL-PE) is related to inappropriate empirical therapy for acute pyelonephritis. The aim of this study was to investigate whether the delay in appropriate antimicrobial therapy of APN caused by ESBL-PE was associated with patient`s poor outcome or not.

Methods. A retrospective cohort study was performed at a tertiary-care hospital from January 2014 through December 2016. Patients who had APN caused by ESBL-PEs and were treated with appropriate definite antibiotics for at least 7 days were enrolled. The delay in appropriates antimicrobial therapy was defined as patients who had received appropriate antibiotics 48 hour or later after diagnosis of APN. Primary endpoint was treatment failure defined as clinical and/or microbiological failure. Secondary endpoint was length of hospital stay and recurrence of febrile urinary tract infection by ESBL-EP within 1-year. The propensity score matching and multivariable Cox proportional hazard modeling were used to adjust heterogeneity of each group.

Results. A total of 175 eligible cases were collected. *Escherichia coli* (144/175, 82.3%) was the most common pathogen, followed by *Klebsiella pneumonia* (29/175,