included. Patients were excluded if < 18 years old, receiving antibiotics for < 24 hours, treated for a polymicrobial BSI, or receiving concomitant antibiotic therapy for another gram-negative (non-ESBL) infection.

Results. One hundred and fourteen patients were analyzed; 74 (65%) patients received CBPN therapy compared with 40 (35%) patients that received a non-CBPN (CEF N=30, PT N=10). There were no statistically significant differences in baseline characteristics between groups. The overall in-hospital mortality rate was 6% (N=7). Eight percent of patients (N=6) in the CBPN arm died compared to 3% (N=1) of patients in the non-CBPN arm, P = 0.42. No difference in mortality was detected between groups when evaluating subgroups with Pitt bacteremia score ≥4 (N=25), requiring ICU admission (N=50), non-genitourinary source (N=50), or by causative organism (N=76 *E. coli*; N=38 *Klebsiella* spp.). There was no difference between groups for secondary outcomes.

Conclusion. CEF and PT are reasonable options for the treatment of ESBL BSI and did not result in increased mortality or decreased clinical efficacy when compared to CBPNs in this cohort.

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

1577. Real-World, Multicenter Experience with Eravacycline for Various Infections

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Eravacycline (ERV) is Food and Drug Administration approved in patients for the treatment of adults complicated intra-abdominal infections in 2018. Real-world data regarding the indications for ERV use are is limited. We evaluated the clinical/safety outcomes of patients treated with ERV in FDA and non-FDA approved indications.

Methods. Multicenter, retrospective, observational study from September 2018 to June 2020. Adult patients treated with ERV for ³ 72 hours were included. The primary outcome was 30-day survival. Secondary outcomes included a lack of 30-day infection-recurrence, resolution of signs/symptoms of infection and safety. All outcomes were measured from ERV start date.

Results. Overall, 108 patients were included from 12 geographically-distinct medical centers across the United States. The median(IQR) age was 60(52-67) years and 60% were male. Median(IQR) APACHE II and Charlson Comorbidity scores were 15(11-21) and 3 (2-6), respectively. The most common sources of infection were intra-abdominal (32%), and respiratory (24%). Common pathogens included *Acinetobacter baumannii* (19%), *Klebsiella pneumoniae* and *Enterococcus faecium* (16%). Infectious diseases consultation was obtained in 98%, and surgical interventions in 51% of cases. Patients often received active therapy prior to ERV(40%). Median(IQR) ERV therapy duration was 7.7(4.4-14.0) days. Among cases with documented cultures, ERV was initiated within a median(IQR) of 4.8(2.5-9.9) days. Combination therapy ³ 48 hours was given in 45%. The primary endpoint was achieved in 79%(85/108). Of patients who died(n=23), 57% were on monotherapy, 39% were critically ill, 39% had intra-abdominal as a source, and 30% had positive blood cultures. For secondary outcomes, 94%(102/108) lacked 30-day infection-recurrence and 74%(80/108) resolved signs/symptoms of infection. ERV was selected primarily for consolidation of the regimen(40%). Eight patients experienced a probable ERV-related adverse event, mainly gastrointestinal(87.5%) and none experienced *clostridium difficile*.

Conclusion. 30-day survival was achieved in the majority of patients treated with ERV. Studies with longer follow-up are required to confirm these findings.

Disclosures. Madeline King, PharmD, Tetraphase (Speaker's Bureau) Bruce M. Jones, PharmD, BCPS, ALK-Abello (Research Grant or Support)Allergan/Abbvie (Speaker's Bureau) Michael J. Rybak, PharmD, MPH, PhD, Paratek (Grant/Research Support)

1578. Treatments for complicated urinary tract infections (cUTI) caused by multidrug resistant (MDR) Gram-negative (GN) pathogens- a systematic review and network meta-analysis (NMA)

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Antimicrobial resistance is a major and growing threat to global public health. Cefiderocol (CFDC) is a new siderophore-cephalosporin with a wide activity spectrum covering all aerobic GN pathogens including all WHO critical priority pathogens, that was recently approved by FDA for the treatment of GN cUTI in susceptible organisms. We aim to understand the relative efficacy and safety of current treatment options for cUTI caused by MDR GN pathogens.

Methods. We conducted a systematic review to identify all relevant trials that investigated the efficacy and safety of antimicrobial regimens, for the treatment of GN pathogens in cUTI. Outcomes of interest included clinical cure and microbiological eradication (ME) at time of cure (TOC) and sustained follow up (SFU), and safety. Evidence networks were constructed using data for outcomes of interest and analyses were conducted in a frequentist framework using NMA methods outlined by the NICE decision support unit using the netmeta package in R.

Results. A total of 5 studies, 6 interventions and 2,349 randomised patients were included in the final analysis. Interventions included CFDC, imipenem-cilastatin (IPM-CIL), ceftazidime-avibactam (CAZ/AVI), doripenem (DOR), levofloxacin and ceftolozane-tazobactam (CEF/TAZ). Trials included predominantly Enterobacterales, and *Pseudomonas aeruginosa* and very few *Acinetobacter baumannii*. The patient population presented some clinical differences across trials, which were not adjusted for the NMA. Overall, there were numerical differences (especially in endpoints at SFU favouring CFDC), but all treatments showed similar efficacy and safety, with exception of higher ME rate at TOC for CFDC vs IPM, Table 1, also observed at SFU, consistent with the data from the individual clinical trial.

Table 1- Results for microbiological eradication

Table 1- Results for microbiological eradication

Comparator	Microbiological eradication at TOC OR (95% CI)* *>1 favours cefiderocol	Microbiological eradication at SFU OR (95% CI)* *>1 favours cefiderocol
ceftolozane-tazobactam	0.83 (0.24 to 2.86)	1.52 (0.61 to 3.80)
ceftazidime-avibactam	1.75 (0.67 to 4.58)	1.52 (0.61 to 3.80)
doripenem	2.44 (0.89 to 6.73)	2.09 (0.80 to 5.47)
imipenem-cilastatin	2.10 (1.33 to 3.32)	1.72 (1.11 to 2.67)
levofloxacin	1.94 (0.61 to 6.17)	-
cefiderocol	Reference	

Conclusion. This NMA, showed superiority of CFDC vs IPM-CIL in ME at TOC and SFU and similar efficacy and safety vs all other comparators, with numeric differences favouring CFDC for outcomes at SFU. These traditional methodologies for NMA, are only valid within a similar pathogens pool and population across the trials, and may not reflect the full value of breadth of coverage that new therapeutic options bring for the treatment of MDR GN pathogens.

Disclosures. Tim Reason, PhD, Shionogi (Consultant) Karan Gill, MSc, Shionogi BV (Employee) Christopher Longshaw, PhD, Shionogi B.V. (Employee) Rachael McCool, PhD, York Health Economics Consortium (Employee, YHEC was commissioned by Shionogi to conduct the systematic review) Katy Wilson, PhD, York Health Economics Consortium (Employee, Shionogi commissioned YHEC to conduct the systematic review) Sara Lopes, PharmD, Shionogi BV (Employee)

1579. *Burkholderia* Returns: Are Two Drugs Better or Back to Bactrim?

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Trimethoprim-sulfamethoxazole (T/S) and levofloxacin are considered first line agents for the treatment of *Burkholderia cepacia complex* (Bcc). Combination therapy (CT) is frequently utilized despite limited clinical evidence supporting this. The objective of this study is to compare outcomes associated with different regimens for the treatment of Bcc infections.

Methods. This is a retrospective cohort study in non-cystic fibrosis adult patients with infection caused by Bcc from 2015 to 2019. The primary outcome is the composite of overall treatment failure defined as clinical failure, microbiologic failure, or mortality at 30 days. Secondary outcomes include mortality, clinical failure, microbiological failure, development of resistance, recurrence, and safety. Comparisons were performed using Chi-squared or Fischer's exact test for categorical variables and Student's t test or the Mann-Whitney U test for continuous variables, as appropriate. Multivariable logistic regression analysis was used to identify independent risk factors for overall treatment failure.

Results. Sixty-eight patients were included, 50 (74%) received monotherapy (MT) and 18 (26%) received CT. MT regimens included meropenem (n=19), ceftazidime (n=15), T/S (n=10), and other (n=6). Various combination regimens were utilized. MT recipients were significantly older, more likely to have renal disease, less likely to have an immunosuppression, and had a higher severity of illness. The most common site of infection was respiratory (78%). No difference was found for overall treatment failure between MT and CT (36.0% vs. 38.9%; p=0.947). No differences were found in the

secondary outcomes (Table 1). Overall treatment failure did not differ by treatment regimens utilized. On multivariable analysis controlling for age, renal disease, CCI, immunosuppression, ICU admission, SOFA score, and receipt of MT, only SOFA score was associated with treatment failure [OR 1.43 (95% CI 1.15 to 1.77); p=0.001] and not MT [OR 1.22 (95% CI 0.25 to 5.97); p=0.808].

Table 1: Treatment Outcomes – MT versus CT

Treatment Outcomes – MT versus CT

Outcome	MT (n=50)	CT (n=18)	P value
Overall treatment failure at 30 days, n (%)	18 (36.0)	7 (38.9)	.947
Clinical failure at 30 days, n (%)	13 (26.0)	5 (27.8)	1.000
Microbiologic failure at 30 days, n (%)	13 (27.1)	4 (23.5)	.972
Development of resistance while on initial treatment regimen, n (%)	4 (30.8)	1 (25.0)	1.000
Recurrence/ongoing infection at 90 days, n (%)	5 (10.0)	1 (5.6)	.569
Mortality at 14 days, n (%)	2 (4.0)	1 (5.6)	1.000
Mortality at 30 days, n (%)	4 (8.0)	2 (11.1)	1.000
Mortality at 90 days, n (%)	10 (27.8)	5 (29.4)	1.000
Discontinuation due to adverse drug reaction, n (%)	4 (8.0)	2 (11.1)	1.000

Conclusion. There were no differences in outcomes between MT and CT groups for the treatment of Bcc infection. Treatment outcomes appeared to be driven primarily by disease severity. Additional studies are needed to identify the optimal treatment regimens.

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

1580. *In Vitro* Activity of Ceftazidime-Avibactam Against Enterobacterales and *Pseudomonas aeruginosa* Collected in Latin America as part of the ATLAS Global Surveillance Program, 2017-2019

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Ceftazidime-avibactam (CAZ-AVI) is a β-lactam/non-β-lactam β-lactamase inhibitor combination with *in vitro* activity against Enterobacterales (Ent) and *Pseudomonas aeruginosa* (*Psa*) carrying Class A, C and some Class D β-lactamases. We examined the *in vitro* activity of CAZ-AVI and comparators against isolates collected in Latin America (LA) as part of the ATLAS surveillance program.

Methods. Non-duplicate isolates of Ent (n=8416) and *Psa* (n=2521) were collected in 10 countries in Central America (CAC; Costa Rica, Dominican Republic, Guatemala, Panama [2018-2019 only]) and South America (SA; Argentina, Brazil, Chile, Colombia, Mexico, Venezuela [2017-2019]). Susceptibility testing was performed by CLSI broth microdilution and values were interpreted using CLSI 2020 breakpoints. CAZ-AVI was tested at a fixed concentration of 4 µg/mL AVI. Isolates with meropenem (MEM) MICs ≥2 µg/mL (Ent) or ≥4 µg/mL (*Psa*) were screened for β-lactamase genes.

Results. CAZ-AVI demonstrated potent *in vitro* activity against Ent collected in LA overall and in the CAC and SA subregions (95-99% susceptible (S)) that was comparable to or exceeded the activity of comparators including MEM, amikacin (AMK) and tigecycline (TGC) (Table). CAZ-AVI retained good activity against MEM non-susceptible (NS) Ent collected in SA (82% S; 6.9% of collected isolates) but activity was reduced against MEM-NS Ent from CAC (10% S; 5.7% of collected isolates), which included a high proportion of isolates carrying NDM-type metallo-β-lactamases (MBL). Among *Psa*, CAZ-AVI showed greater activity than the tested comparators against both all (86-92% S) and MEM-NS (61-66% S) isolates collected in LA overall and in the two subregions.

Table

		Drug/Percent susceptible (%)					
Organism/Region	Phenotype (n)	CAZ-AVI	CAZ	MEM	TZP	AMK	TGC
Ent/LA	All (n=8416)	98.2	67.9	93.2	82.7	96.2	97.2
	MEM-NS (n=570)	74.7	5.4	0.0	1.9	70.2	95.6
CAC	All (n=1058)	94.9	69.9	94.3	85.4	95.8	98.1
	MEM-NS (n=60)	10.0	1.7	0.0	1.7	48.3	98.3
SA	All (n=7358)	98.6	67.6	93.1	82.4	96.2	97.1
	MEM-NS (n=510)	82.4	5.9	0.0	2.0	72.8	95.3
Psa /LA	All (n=2521)	87.0	71.5	66.9	69.1	82.1	NA
	MEM-NS (n=835)	61.9	35.3	0.0	28.6	52.3	NA
CAC	All (n=348)	92.2	81.6	78.2	79.3	85.9	NA
	MEM-NS (n=76)	65.8	44.7	0.0	31.6	48.7	NA
SA	All (n=2173)	86.1	69.9	65.1	67.5	81.5	NA
	MEM-NS (n=759)	61.5	34.4	0.0	28.3	52.7	NA

LA, Latin America (includes all countries in CAC and SA); CAC, Central American Countries (Costa Rica, Dominican Republic, Guatemala, Panama; isolates collected in 2018-2019 only); SA, South America (Argentina, Brazil, Chile, Colombia, Mexico, Venezuela; isolates collected in 2017-2019). CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; TZP, piperacillin-tazobactam; AMK, amikacin; TGC, tigecycline; NS, non-susceptible; NA, no CLSI interpretive criteria are available for this organism/drug combination.

Conclusion. CAZ-AVI showed potent *in vitro* activity against Ent and *Psa* collected from patients in the CAC and SA subregions of LA. Activity was also good against MEM-NS isolates from SA but was reduced against MEM-NS Ent from CAC that included a high proportion of MBL-positive isolates. The regional and country prevalence of different carbapenem-resistance mechanisms must be considered when evaluating treatment options; however, CAZ-AVI could provide a valuable therapeutic option for treatment of infections caused by Ent and *Psa* in LA.

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1581. *In Vitro* Activity of Ceftolozane/Tazobactam against *Pseudomonas aeruginosa* from ICU and Non-ICU Patients with Respiratory Tract Infections in the Asia/Pacific region – SMART 2016-2018

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Ceftolozane/tazobactam (C/T) is an antipseudomonal cephalosporin combined with a β-lactamase inhibitor approved by FDA and EMA for hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP). Elevated antimicrobial resistance rates have been reported among pathogens collected in ICUs. Using isolates collected in Asia/Pacific as part of the global SMART surveillance program, we evaluated the activity of C/T and comparators against *P. aeruginosa* from patients with respiratory tract infections (RTI) in ICU and non-ICU wards.

Methods. In 2016-2018, 55 clinical laboratories in 11 Asia/Pacific countries collected 2530 *P. aeruginosa* isolates from RTI. MICs were determined using CLSI broth microdilution and interpreted with CLSI breakpoints. C/T-nonsusceptible isolates (except those from India) were screened by PCR and sequencing for genes encoding β-lactamases.

Results. Susceptibility to C/T in Asia/Pacific was 85.3% in ICUs and 92.2% in non-ICUs, 15-23 percentage points and 13-19 percentage points, respectively, higher than to meropenem, cefepime, and piperacillin-tazobactam. C/T maintained activity against 58.8% and 69.4% of meropenem-nonsusceptible isolates from ICU (n=294) and non-ICU patients (n=346), respectively. Acquired β-lactamases were detected in 64% of C/T-nonsusceptible isolates from ICUs (n=90; 54% MBL-positive, 1% GES carbapenemase-positive, 9% ESBL-positive) and in 47% of C/T-NS isolates from non-ICUs (n=86; 33% MBL-positive, 6% GES-carbapenemase-positive, 8% ESBL-positive). The table presents country-level rates of C/T-susceptible and carbapenemase-positive *P. aeruginosa* for countries with n >20 in both ICU and non-ICU subsets.

Table

	ICU		Non-ICU	
Country (n ICU | n non-ICU)	% C/T-Susceptible	% Carba-penemase+	% C/T-Susceptible	% Carba-penemase+
Australia (127|314)	97.6	0.8	97.1	0.0
India (86|94)	50.0	N/A	57.5	N/A
South Korea (84|168)	96.4	0.0	93.5	1.2
Malaysia (61|139)	91.8	0.0	98.6	0.7
New Zealand (36|179)	97.2	0.0	96.7	0.6
Philippines (29|65)	93.1	3.4	95.4	3.1
Taiwan (283|405)	95.1	0.0	96.5	0.2
Thailand (87|169)	74.7	13.8	86.4	7.1
Vietnam (86|34)	59.3	40.7	52.9	44.1

N/A, not available

Conclusion. In Asia/Pacific overall, C/T maintained susceptibility rates >85% in both ICU and non-ICU wards against *P. aeruginosa* isolates from RTI, with rates >91% in most countries. Susceptibility was lower in countries with higher rates of carbapenemase-positive *P. aeruginosa*. C/T could provide an important treatment option for RTI infections caused by *P. aeruginosa* in the Asia/Pacific region.

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1582. *In Vitro* Activity of Ceftolozane/Tazobactam against Enterobacterales and *Pseudomonas aeruginosa* Isolates from Geriatric Patients in the Asia/Pacific region – SMART 2016-2018

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