These data suggest that MIN remains a useful treatment option for infections caused by unusual NFGN.

Activities of MIN when tested against NFGN isolates

Organism	No. of isolates	MIC_{50}	MIC_{90}	CLSI[a]		
				%S	%I	%R
Achromobacter xylosoxidans	202	1	4	92.1	5.0	3.0
Burkholderia cepacia species complex	199	2	>8	85.9	4.5	7.0
Unspeciated *Achromobacter*	190	1	4	92.6	6.3	1.1
Aeromonas spp [b]	127	0.5	2	99.2	0.0	0.8-
Chryseobacterium spp [c]	59	2	4	94.9	5.1	0.0
Alcaligenes faecalis	42	2	8	88.1	7.1	4.8

[a] CLSI (2020).
[b] Using M45 (CLSI, 2015) tetracycline breakpoints of ≤4/8/≥16mg/L. Organisms include: *Aeromonas caviae* (10), *A. hydrophila* (35), *A. sobria* (1), *A. veronii* (10), unspeciated *Aeromonas* (71).
[c] Organisms include: *Chryseobacterium gleum* (18), *C. hominis* (1), *C. indologenes* (31), unspeciated *Chryseobacterium* (9).

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1621. Novel Beta-lactam Beta-lactamase Inhibitors Against Alternative Antibiotics for the Treatment of Complicated Urinary Tract Infections and Pyelonephritis Caused by Carbapenem-resistant *Enterobacterales*

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. There is little data on the comparative efficacy or safety of carbapenem-resistant *Enterobacterales* (CRE)-targeted beta-lactam beta-lactamase inhibitors (BL-BLI), including ceftazidime/avibactam (CZA) and meropenem/vaborbactam (MVB), versus alternative antibiotics for the treatment of CRE complicated urinary tract infections/acute pyelonephritis (cUTI/AP). The objective of this study was to evaluate rates of clinical failure in patients with CRE cUTI/AP treated with CRE-targeted BL-BLI vs. alternative regimens.

Methods. This was a multicenter, retrospective cohort study of adults admitted with a CRE cUTI/AP treated with CRE-active antibiotic(s), including combination therapy, for at least 48 hours between January 2012 and June 2019. Exclusion criteria included CRE colonization, non-urinary source co-infection, non-*Enterobacterales* cUTI/AP, or mortality within 48 hours of index culture. The primary outcome was clinical failure, defined as continued symptoms or recurrence at 30 days from index culture. Secondary outcomes included 90-day recurrence and 30-day readmission. Safety outcomes included treatment-limiting adverse effects, non-treatment limiting nephrotoxicity, and *C. difficile* infection.

Results. A total of 47 patients were included (BL-BLI, n=16; alternative, n=31). Alternative regimens contained aminoglycosides, carbapenems, polymyxins, and tigecycline and utilized combination therapy more often (32.3% vs. 6.3%, p=0.046). Clinical failure occurred in 12.5% of patients in the BL-BLI group vs. 38.7% in the alternative group (p=0.063). Higher rates of 90-day recurrence (25.8% vs. 18.8%) and 30-day readmissions (51.6% vs. 31.3%) occurred in the alternative group vs. the BL-BLI group but were not statistically significant (Table 2). There were clinically significant rates of nephrotoxicity in the alternative group (45.2%) compared to the BL-BLI group (18.8%), contributing largely to the difference in treatment-limiting adverse effects (29% vs. 0%, p=0.017).

Table 1: Antibiotic Data

Table 1: Antibiotic Data	Total (N=47)
BL-BLI-based regimen [n (%)]	16 (34.0)
Monotherapy	15 (93.8)
Ceftazidime-avibactam	11 (73.3)
Meropenem-vaborbactam	4 (26.7)
Combination therapy	1 (6.25)
CZA + Aminoglycoside	1 (100.0)
Alternative regimen [n (%)]	31 (83.8)
Monotherapy	21 (67.7)
Aminoglycoside	8 (38.1)
Tigecycline	8 (38.1)
Polymyxins	3 (14.3)
Carbapenems	1 (4.8)
Fluoroquinolones	1 (4.8)
Combination therapy	10 (32.3)
Aminoglycoside + Carbapenem	3 (30.0)
Tigecycline + Carbapenem	3 (30.0)
Tigecycline + Polymyxins	3 (30.0)
Polymyxins + Minocycline	1 (10.0)

Abbreviations: BL-BLI, beta-lactam beta-lactamase inhibitor; CZA, ceftazidime-avibactam

Table 2: Efficacy Outcomes

Table 2: Efficacy Outcomes	BL-BLI (n=16)	Alternative (n=31)	*p*-value
Clinical failure [n (%)]	2 (12.5)	12 (38.7)	0.063
30-day recurrence [n (%)]	1 (50.0)	3 (25.0)	
Persistent symptoms despite therapy [n (%)]	1 (50.0)	9 (75.0)	
90-day recurrence [n (%)]	3 (18.8)	8 (25.8)	0.59
Emergence of prior study drug(s) resistance on repeat urine culture (%)]	0 (0)	1 (12.5)	NS
30-day all-cause readmission [n (%)]	5 (31.3)	16 (51.6)	0.18
Index infection-related [n (%)]	0 (0)	8 (50)	0.055
30-day all-cause mortality [n (%)]	1 (6.3)	2 (6.5)	0.99
Length of hospital stay (days) (median [IQR])	12.5 [7.5,17.0]	11.0 [7.0,19.0]	NS

Abbreviations: BL-BLI, beta-lactam beta-lactamase inhibitor; CZA, ceftazidime-avibactam

Table 3: Safety Outcomes

Table 3: Safety Outcomes	BL-BLI (n=16)	Alternative (n=31)	*p*-value
Treatment-limiting adverse effect [n (%)][a]	0 (0)	9 (29.0)	0.017
Nephrotoxicity	0 (0)	8 (88.9)	0.96
Stage I[b]	0 (0)	6 (75)	
Stage II[c]	0 (0)	1 (12.5)	
Stage III[d]	0 (0)	1 (12.5)	
Ototoxicity	0 (0)	1 (11.1)	
Non-treatment limiting nephrotoxicity [n (%)]	3 (18.8)	6 (19.4)	
C.difficile infection [n (%)][e]	1 (6.3)	2 (6.5)	0.99

[a]Treatment-limiting adverse events: that resulted in a change in therapy while on study-drug
[b]AKIN Stage I: Increase in serum creatinine x 1.5 or at least 0.3 mg/dL
[c]AKIN Stage II: Increase in serum creatinine x 2
[d]AKIN Stage III: Increase in serum creatinine x 3 or at least 4 mg/dL (with acute rise of at least 0.5 mg/dL), or initiation or renal replacement therapy
[e]*Clostridioides* difficile infection: within 90 days of the initiation of antibiotics

Conclusion. In this retrospective study, no difference in clinical failure resulted among groups; however, there was significantly more treatment-limiting adverse effects in the alternative group compared to the BL-BLI-based regimens, driven by nephrotoxicity.

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1622. Outcomes of Colistin Weight-Based Dosing Versus The Non-Weight-Based Dosing

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. The use of colistin is currently the mainstay antimicrobial for several multi-drug resistant organisms (MDROs). New guidelines were recently published recommending non-weight-based (NWB) dosing of colistin. There is limited data on

outcomes with this new dosing strategy. The purpose of this study was to investigate the outcomes of the new NWB dosing strategy in comparison to the previously used weight-based (WB) dosing strategy.

Methods. A retrospective study was conducted at our quaternary care hospital between January 2016 and April 2020. Adults (≥ 18 years), who received intravenous (IV) colistin for ≥ 72 hours were included. Documented clinical cure was the primary endpoint, which was defined as having at least two of the following: normalization of white blood cell count or ≥ 25% reduction, defervescence, hemodynamic stability, normalization of inflammatory markers (C-reactive protein and procalcitonin values) or ≥ 25% reduction, or the resolution of signs and symptoms of infection by the end of the therapy. Secondary outcomes were microbiological cure, incidence of acute kidney injury (AKI), time to AKI, outcomes of AKI, time to AKI recovery, new infection while on IV colistin, recurrence of infection, and all-cause mortality.

Results. A total of 104 primarily male (57.7%) patients with a mean age of 63 ± 20.23 years and weight of 70.24 ± 19.46 kg met the inclusion criteria. At baseline for both groups, the estimated creatinine clearance was 74.23 ± 70.86 mL/min and renal replacement therapy was observed in 34.62%. There was no statistically significant difference observed in clinical cure rate in the WB was 77.03% while 83.33% in the NWB (p-value 0.48). However, a higher rate of AKI was observed in NWB was 84.21% while 53.33% in WB (p-value 0.02). Amongst those who had AKI, NWB had better AKI recovery status with 60.00% while 17.95% in WB (p-value 0.00). A higher all-cause mortality rate was observed in the WB group with 55.41% while 20.00% in NWB (p-value 0.02).

Conclusion. The study showed no statistical difference in the primary outcome between the two groups, however, higher AKI rates, AKI recovery and all-cause mortality was observed in non-weight-based dosing when compared to the weight-based dosing. Our data needs to be validated in a larger study.

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

1623. Outcomes of Critically Ill Adults, Hospitalized Patients (Pts) with *Pseudomonas aeruginosa* (PSA) Hospital- and Ventilator-Associated Pneumonia (HAP/VAP) Who Received an Active Anti-Pseudomonal β-Lactam (ASPB): Does "S" Equal Success in the Presence of Resistance to other ASPB?

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. The most commonly prescribed antibiotics for PSA HAP/VAP are ASPBs: meropenem (MER), piperacillin/tazobactam (TZP),cefepime (FEP) and ceftazidime (CAZ). Similar resistance mechanisms in PSA affect these agents, and it is unclear if you can use a susceptible ASPB when the PSA is resistant to other ASPBs. This study evaluates the impact of ASPB resistance among pts with PSA HAP/VAP who initially received therapy with an ASPB to which PSA was susceptible.

Methods. A cohort study of Kaiser Permanente Southern California (KPSC) members (1/1/11-12/31/17) was performed. Inclusion criteria: (1) age ≥ 18 years; (2) HAP/VAP diagnosis; (3) monomicrobial PSA on a clinical respiratory culture (index PSA); (4) ICU at index PSA; (5) received MER, TZP, FEP or CAZ within ≤ 2 days of index PSA; (6) index PSA was susceptible to ASPB received; (7) no cystic fibrosis; (8) survived > 2 days post index PSA, and (9) ≥ 6 months of KPSC membership prior to index PSA. Pts were stratified by presence of resistance to MER, TZP, and FEP on index PSA (0 vs. ≥1 resistant ASPB). Outcomes: 30-day mortality and discharge to home.

Results. 560 patients were included. Mean (SD) age was 70.5 (14.2) years, 60% were male, and most had many comorbidities. Thirty-day mortality was 28%, and 32% were discharged home. Ninety-five (17%) received an active ASPB for PSA HAP/VAP that was resistance to ≥ 1 ASPB. Relative to pts with no ASPB resistance, pts with resistance ≥ 1 ASPB had higher 30-day mortality (32% vs. 27%) and were less likely to be discharged home (17% vs. 35%). In multivariate analyses, pts with resistance ≥ 1 ASPB had higher 30-day mortality (aOR=1.61 [CI: 1.01-2.56]) and were less likely to be discharged home (aHR [95%]: 0.5 [0.3-0.9]).

Crude and Adjusted Associations Between Presence of Anti-Pseudomonal β-Lactam -Resistance (Reference= no ASPB resistance) and Outcomes among Adult, ICU patients with HAP/VAP due to PSA who received a Microbiologic Active Anti-Pseudomonal β-Lactam

	Crude OR (95% CI)[a]	Adjusted OR (95% CI)[b], IPTW
30-day mortality	1.27 (0.79-2.05)	1.61 (1.01-2.56)
	Crude HR (95% CI)[c]	**Adjusted HR (95% CI)[d], IPTW**
Discharged home	0.43 (0.26-0.73)	0.54 (0.33-0.89)

Abbreviations: SNF, skilled nursing facility; IPTW, inverse probability treatment weighting; HR, hazard ratio; OR, odds ratio; CI, confidence interval

[a.] OR (95% CI) calculated by logistic regression

[b.] OR (95% CI) calculated by logistic regression with IPTW, adjusting for age, gender, race/ethnicity, SNF transfer, invasive devices, Pseudomonas exposure 30 days prior to index culture, prior 6-month hospitalization, LOS from admission to index culture, select comorbidities (myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, diabetes with complications, cancer, other immune condition), severity risk score (COPS2), prior 30-day antibiotics, prior antibiotics for Pseudomonas, WBC, eGFR.

[c.] HR (95% CI) calculated using proportional hazard Cox regression

[d.] HR (95% CI) calculated using proportional hazard Cox regression with IPTW, adjusting for age, gender, race/ethnicity, SNF transfer, invasive devices, Pseudomonas exposure 30 days prior to index culture, prior 6-month hospitalization, LOS from admission to index culture, select comorbidities (myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, diabetes with complications, cancer, other immune condition), severity risk score (COPS2), prior 30-day antibiotics, prior antibiotics for Pseudomonas, WBC, eGFR.

Conclusion: Despite receiving a microbiologic active agent within ≤ 2 days of their PSA HAP/VAP, pts with PSA that were resistant to ≥ 1 ASPB had worse outcomes relative to those that had no ASPB resistance. Further study is needed, but these findings suggest that the full ASPB susceptibility profile needs to be considered when selecting therapy for pts with PSA HAP/VAP. More studies are also needed to determine if alternative or combination therapies may be needed to maximize outcomes in PSA infection when there is resistance ≥ 1 ASPB.

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1624. Real World Experience with Daptomycin (DAP) and Ceftaroline (CPT) Combination Therapy for Methicillin-resistant Staphylococcus aureus (MRSA) bacteremia

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Methicillin-resistant *Staphylococcus aureus* bacteremia is associated with significant mortality rates up to 30%. Guideline-recommended first-line therapy includes monotherapy with either vancomycin or DAP. Alternative regimens are recommended for persistent MRSA bacteremia of ≥ 7 days or earlier if evident clinical deterioration. The combination of DAP plus CPT has been investigated as salvage therapy due to its synergistic mechanism potential, but real-world data with the combination therapy is limited. The aim of this study was to evaluate the efficacy of DAP plus CPT combination therapy for the treatment of MRSA bacteremia and identify independent predictors of 30-day mortality.

Methods. This was a single center retrospective study of patients receiving DAP-CPT at any point in therapy for the treatment of MRSA bacteremia. Univariable and multivariable analyses were performed to identify independent predictors of 30-day mortality.

Results. Sixty-five unique patients received DAP-CPT with a median time to combination therapy of 7 days. There were no significant independent predictors of 30-day mortality. The most common reason for combination therapy was persistent