Results. We included 250 patients during the study period. The median age was 55 (19–91) years, 55.6% (139/250) were male, and 49.2% (123/250) were admitted to the intensive care unit (ICU). 77.2% (193/250) had at least one comorbidity, with solid-organ malignancy (27.6%, 69/250) being the most common. Most patients had at least one invasive device; commonly a nasogastric tube (64.4%, 161/250) or mechanical ventilator (63.2%, 158/250). There was an increase in Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II score, qSOFA, and septic shock from baseline to 24 hours prior to colistin use (Table 1). The most common site of infection was the respiratory tract (90.8%, 227/250). Majority of patients (78.8%, 197/250) had Acinetobacter baumannii infection of which 79.9% were extensively drug-resistant (XDR), susceptible only to colistin and amikacin or minocycline. Colistin was given for a mean of 12 (2-43) days, concomitant with meropenem in 96.4% (241/250). Most patients received piperacillin-tazobactam (59%, 142/250) and/or meropenem (58%, 138/250) within the same admission. Nephrotoxicity was a common adverse effect. The clinical success rate was modest and overall mortality was 41.6% (104/250).

Conclusion. Colistin was frequently used in combination with a carbapenem for treatment of XDR-related respiratory infection or septic shock. Nephrotoxicity was a common adverse effect. The clinical success rate was modest and overall mortality was high.

Table 1. Septic shock, Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II, and quick Sequential Organ Failure Assessment (qSOFA) score

| Scoring Criteria | n=250 | Frequency (%) | Mean ± SD |
|------------------|-------|---------------|-----------|
| Septic shock     |       |               |           |
| Baseline         | 13    | 5.2           |           |
| 24 hours prior to colistin | 40 | 16            |           |
| APACHE II        |       |               |           |
| Baseline         | 13.5±3.4 |           |           |
| 24 hours prior to colistin | 16.0±7.43 |           |           |
| qSOFA            |       |               |           |
| Baseline         | 1.00 ±0.87 |           |           |
| 0                | 82    | 32.8          |           |
| 1                | 99    | 39.6          |           |
| 2                | 56    | 22.4          |           |
| 3                | 13    | 5.20          |           |
| 24 hours prior to colistin | 1.40±10.97 |           |           |
| 0                | 51    | 20.4          |           |
| 1                | 83    | 33.2          |           |
| 2                | 80    | 32.0          |           |
| 3                | 36    | 14.4          |           |
| Day 7 of colistin | 0.97±3.06 |           |           |
| 0                | 111   | 44.4          |           |
| 1                | 68    | 27.2          |           |
| 2                | 39    | 15.6          |           |
| 3                | 32    | 12.8          |           |

Table 2. Adverse Events

| Toxocities         | n=250 | Frequency (%) | Mean ± SD |
|--------------------|-------|---------------|-----------|
| Nephrotoxicity     | 77    | (30.8)        |           |
| AKI Stage 1        | 27    | (10.8)        |           |
| AKI Stage 2        | 20    | (8.0)         |           |
| AKI Stage 3        | 30    | (12.0)        |           |
| CRRT               | 15.6  | (6.2)         |           |
| Neurotoxicity      | 11.0  | (4.4)         |           |
| Hypersensitivity   |       |               |           |
| (AKI) Acute Kidney Injury (Based on Kidney Disease: Improving Global Outcomes criteria), RRT: Renal Replacement Therapy |

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522. In Vitro Antimicrobial Activity of Ceftazidime/Avibactam Compared with Ceftolozane-Tazobactam Against Real-world Clinical Isolates of Pseudomonas aeruginosa at a Large Academic Tertiary Care Hospital

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Session: 56. HAI: MDRO – GNR Treatment
Thursday, October 3, 2019: 12:15 PM

Background. Ceftazidime/avibactam (CZA) and ceftolozane-tazobactam (CT) are new additions to the antibiotic armamentarium with activity against gram-negative pathogens, most notably drug-resistant Pseudomonas aeruginosa (PSA). The purpose of this study was to compare the in vitro activity of CZA and CT against a large real-world sample of clinical isolates of PSA displaying different phenotypes of resistance to conventional β-lactams at an institution where both CZA and CT are routinely tested on all isolates.

Methods. All cultures from patient infections with PSA from May 2018 to February 2019 at Michigan Medicine were included. Minimum inhibitory concentrations (MICs) were determined using TREK broth microdilution panels and isolates were considered susceptible to MV if the MIC was ≤4 mg/L and MEM if the MIC was ≤2 mg/L.

Results. A total of 2,976 isolates of PSA from clinical specimens were included. 50.5% of isolates were susceptible to MEM (MIC ≤1 mg/L and MIC ≤8 mg/L, range ≤1 to >32 mg/L) at a breakpoint of ≤2 mg/L and 86.3% at a breakpoint of ≤4 mg/L; whereas 90.8% of isolates were susceptible to MV (MIC ≤1 mg/L and MIC ≤4 mg/L, range ≤1 to >8 mg/L). Of those displaying MEM MIC >2 mg/L, 53% (n = 308) were susceptible to MV. Of those displaying MEM MIC >4 mg/L, 33.7% (n = 137) were susceptible to MV. Although the majority of MIC discordances in MEM-R/MV-S isolates were 1–2 doubling dilutions, 52 (38%) isolates had their meropenem MIC decreased ≥3 doubling dilutions by the addition of vaborbactam suggesting significant inhibitory activity (Table 1).

Conclusion. We found a surprising number of PSA isolates with discordant MIC and MEM susceptibility at Michigan Medicine. Further exploration of mechanisms of meropenem resistance in these isolates is warranted.

Table 1: Susceptibility discordance by number of doubling dilutions for PSA isolates with MEM MIC >4 mg/L and susceptible to MV

| MEM® MIC | MV® Susceptibility |
|----------|--------------------|
| 1        | d1 dilution        |
| 4        | 1 mg/L, 64         |
| 8        | 4 mg/L, 2 mg/L, 14 |
| 16       | 4 mg/L, 2 mg/L, 12 |
| 32       | 4 mg/L, 2 mg/L, 1 |
| >32      | ≤4 mg/L, 3         |

*Numbers in the table represent MV MICs and number of respective PSA isolates characterized by number of doubling dilutions away from MEM MIC shown in the first column

The lowest doubling dilution of MV tested on the available TREK panel was ≤1 mg/L. Thus, in isolates with MV MIC ≤1 mg/L, the discordance between MV and MEM by doubling dilution represents the minimum potential difference.

The highest doubling dilution of MEM tested on the available TREK panel was ≥32 mg/L. Thus, an MIC of 64 mg/L was used as a surrogate to calculate the number of isolates with discordant MIC and MEM. The discordance represented in the table therefore represents the minimum potential difference.

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to CZA. Our findings are unique compared with other published reports where CT has consistently demonstrated greater activity than CZA against resistant *P. aeruginosa* and suggest routine testing of both CT and CZA should occur.

### Table 1: Comparison of CZA and CT susceptibility, MIC50, MIC90, and range among PSA isolates

| CZA               | CT          | MIC50 | MIC90 | MIC Range (mg/L) |
|-------------------|-------------|-------|-------|------------------|
| **All isolates**  |             |       |       |                  |
| 2972              | 96.1        | 8     | 8-16  | 1.0              |
| **PEP-CAZ/PTD/ MEMS** | 2081       | 100   | 4     | 16-32            |
| **PEP**           | 51          | 100   | 8     | 16-32            |
| **CAZ**           | 7           | 85.7  | 8-16  | 16-32            |
| **PTD**           | 87          | 100   | 8     | 8-16             |
| **MEMS**          | 144         | 100   | 8     | 8-16             |
| **PEP-CAZ/R**     | 6           | 88.1  | 4     | 16              |
| **PEP-PTD/R**     | 20          | 100   | 4     | 8-16            |
| **PEP/CAZ/R**     | 15          | 100   | 4     | 8-16             |
| **CAZ-PTD/R**     | 57          | 100   | 8     | 8-16             |
| **CAZ-MEMS**      | 3           | 100   | 8     | 8-16             |
| **PTD-MEMS**      | 134         | 100   | 8     | 8-16             |
| **PEP-CAZ/PTD/MEMS** | 75        | 76.7  | 4     | 16-32          |
| **PEP**           | 8           | 62.5  | 4     | 16              |
| **CAZ-PTD/MEMS**  | 25          | 88    | 4     | 16              |
| **PTD/CAZ-R**     | 60          | 96.7  | 4     | 8-16             |
| **CAZ-R**         | 237         | 59.4  | 3     | 16-32            |

### Table 2: CZA susceptibility stratified by CT susceptibility

| CZA-S (n=2859) | 2775 | 84 |
|----------------|------|----|
| CZA-R (n=113)  | 24   | 89 |

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524. Understanding the Treatment of Carbapenem-Resistant Enterobacteriaceae (CRE) Infections in the United States (US): Insights from a Survey of Hospital-Based Pharmacists

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**Session:** 56. HAI: MDRO – GNT Treatment

**Thursday, October 3, 2019: 12:15 PM**

**Background.** New anti-CRE antibiotics (ceftazidime–avibactam, C-A; meropenem–vaborbactam, M-V; plazomicin, PLZ) are associated with improved outcomes and lower toxicities than polymyxins (PMs; colistin; polymyxin B) in treating CRE infections. We previously demonstrated that ~40% (range: 28-71%) and ~23% (16–41%) of CRE infections in the United States were treated with PMs or new agents, respectively, as of 1/19.

**Aims.** To understand formulary status, availability and positioning of new anti-CRE agents and PMs, we surveyed hospital-based Society of ID Pharmacists (SIDP) members (11–12/18; Qualtrics).

**Results.** There were 218 respondents from 41 states. Mean CRE infections encountered were 2.7/mo (8-36). C-A, M-V, PLZ were formulary restricted or non-formulary but available at 84%, 68% and 31% of hospitals, respectively; agents were stocked at 90%, 26% and 9% in CRE pneumonias (PNA), bacteremia (BSI), abdominal (IAI) and urinary infections by 76%, 96% and 87% at hospitals with a new agent stocked (P = .009).

**Conclusions.** New agents are positioned as the first line against CRE PNA, BSI and IAI at most US hospitals with an SIDP member pharmacist, but they are still prescribed less against CRE infections than PMs nationally. Smaller hospitals are less likely to have a new agent stocked (P = 0.005), and less likely to have a new agent stocked (P = 0.005) or to position a new agent as first line against CRE PNA, BSI and IAI (P = 0.009). Similar associations were not evident by hospital type (academic, community teaching, or non-teaching).

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523. Dual vs. Triple Antibiotic Therapy for Carbapenem-Resistant Acinetobacter baumannii Infections

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**Session:** 56. HAI: MDRO – GNT Treatment

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**Background.** Infections caused by carbapenem-resistant *Acinetobacter baumannii* (CRAB) remain some of the most difficult to treat due to extremely high rates of resistance. The purpose of this study was to compare the efficacy of dual vs. triple targeted antibiotic regimens for CRAB infections.

**Methods.** This was an IRB approved retrospective cohort study performed at a 607-bed community health system between January 2016 and December 2018. Patients were included in the analysis if they were ≥18 years old and received antibiotics for CRAB for ≥272 hours. Patients were excluded if they were pregnant and had CRAB isolated solely from the urine. The primary endpoints of the study were differences in all-cause in-hospital mortality (ACIM) and clinical cure (CC) rates for patients treated with dual vs. triple antibiotic therapy. The secondary endpoint result focused on the difference in length of stay (LOS) between treatment groups. A sub-group analysis was performed for patients treated with ticagrelor vs. minocycline combination therapy to determine differences ACIM and CC, and LOS. A multi-logistic regression analysis (MLRA) was performed to determine patient factors that were associated with ACIM and CC.

**Results.** A total of 32 patients were included in the primary analysis. No difference was seen in ACIM between dual vs. triple antibiotic groups (9.5% vs. 18.2%, P = 0.59). CC (63.6% vs. 57.1%, P = 1.0) and LOS (12 vs. 11 days, P = 1.0) was similar amongst patients treated with dual vs. triple antibiotic group. No differences were seen in ACIM (15.4% vs. 16.7%, P = 1.0), CC (86.3% vs. 69.2%, P = 1.0) and LOS (15 vs. 14 days, P = 1.0) between ticagrelor and minocycline combination therapy groups. The MLRA revealed a positive association with increased serum creatinine and ACIM (OR 3.29, 95% CI 1.35–8.04; P = 0.009) as well as shorter time to appropriate antibiotic therapy and clinical cure (OR 1.49, 95% CI 1.02–2.20; P = 0.04). CRAB isolates were more likely to be susceptible to minocycline vs. ticagrelor (83% vs. 18%, P = 0.003).

**Conclusion.** No differences were seen in ACIM, CC and LOS between dual vs. triple antibiotic groups. Minocycline tends to sustain better susceptibility toward CRAB vs. ticagrelor. Elevated serum creatinine was found to be a predictor for ACIM while shorter time to appropriate antibiotic therapy was associated with CC.

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