Background. Infections due to extended spectrum β-lactamase (ESBL) producing bacteria are problematic due to the association with worse outcomes and limited treatment options. Carbapenems (CBPs) remain the drugs of choice for these infections due to evidence of a mortality benefit and the mixed clinical efficacy associated with piperacillin/tazobactam (PTZ) despite often reported *in vitro* activity. While definitive treatment for these infections has been well-defined, evidence for appropriate empiric therapy remains inconclusive. Rapid molecular assays capable of identifying ESBL markers may aid in switching to appropriate definitive therapy sooner and spare empiric carbapenem use.

Methods. This multicenter retrospective study at 9 sites at Baylor Scott & White Health included patients with a positive blood culture with ESBL-producing bacteria identified by rapid molecular assay from January 1, 2014 to September 22, 2017 and were empirically prescribed either PTZ or a CBP. Patients were excluded if they continued PTZ for more than 24H after identification or did not receive a CBP for definitive therapy. Categorical data were analyzed using the Fisher's exact test and continuous data were evaluated using the t-test and Wilcoxon rank-sum test.

Results. 117 patients met inclusion criteria of which 66 and 51 received empiric PTZ or CBPs, respectively. Baseline characteristics were similar between the groups, including suspected source of bacteremia, prior hospital stay, prior antibiotic therapy, history of positive non-blood ESBL culture, ICU admission, and time to ESBL identification. There was no difference in hospital mortality (3 vs. 7.8%, $P = 0.4$), hospital length of stay (6.1 vs. 5.9%, $P = 0.88$), ICU length of stay (4.7 vs. 3.3%, $P = 0.39$) or recurrent ESBL bacteremia (7.6 vs. 7.8%, $P = 0.99$) between those that received PTZ or a CBP for initial treatment, respectively.

Conclusion. This study in patients with ESBL bacteremia showed similar outcomes when treated empirically with PTZ or a CBP. In the era of rapid molecular assays, these results suggest that empiric PTZ use and avoidance of empiric CBP therapy in the first 24H of infection can be considered until a microbiological diagnosis is confirmed.

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

2443. Searching for the Optimal Treatment Regimen for Metallo-β-Lactamase Producing *Enterobacteriaceae*: Aztreonam Plus Ceftazidime–Avibactam vs. Aztreonam Plus Meropenem–Vaborbactam

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Session: 250. Treatment of AMR Infections
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Background. Pathogens harboring metallo-β-lactamase (MBL) enzymes pose a large threat to public health. Aztreonam (ATM) is not hydrolyzed by MBLs but is inactivated by other β-lactamases, which are often co-harbored in MBL-producers. Ceftazidime/avibactam (CAZ/AVI) and meropenem/vaborbactam (MER/VBR) are novel β-lactam/β-lactamase inhibitors (BL/BLI) with potent activity against serine β-lactamase producing *Enterobacteriaceae*. Combining ATM with BL/BLI agents may provide activity against *Enterobacteriaceae* producing serine and MBLs.

Methods. Two clinical *E. coli* isolates were used. MICs were determined in triplicate and modal values are reported. Time kill analyses were performed in triplicate at standard inoculum (10^6). Each agent was tested alone and in combination at either *f*Cmax or ¼, ½, 1, 2, or 4× MIC based on susceptibility. Bactericidal activity was ≥3 $\log_{10}$ reduction in CFU/mL from the starting inoculum. Synergy was ≥2 $\log_{10}$ reduction in CFU/mL compared with the most active agent alone. Antagonism was ≥2 $\log_{10}$ increase in CFU/mL compared with the most active agent alone.

Results. Genotypic/phenotypic susceptibilities are in Table 1. Against EC-1, ATM alone at *f*Cmax had no activity. When combined with CAZ/AVI or MER/VBR, respectively, synergy was observed with average $\log_{10}$ decrease in CFU/mL at 24 hours of 3.92 and 5.04 (Figure 1a). Synergy seemed to be driven solely by the addition of the BLI as ATM/CAZ and ATM/MER did not demonstrate synergy (Figure 1a). Against EC-2, ATM alone at 1/4× MIC showed no activity (Figure 1b). Combining ATM with either CAZ/AVI or MER/VBR did not improve the activity or demonstrate synergy (Figure 1b). Interestingly, removing CAZ significantly improved the activity of ATM/AVI.

Conclusion. There were no significant differences in activity or synergy observed between the combinations of ATM with either CAZ/AVI or MER/VBR against serine- and MBL-producing *E. coli*. Synergy appears to be driven by the ATM-BLI combinations, with ATM-AVI demonstrating more consistent synergy than ATM-VBR. Further studies including more isolates and combinations are warranted.

	EC-1 (NDM, CMY2/FOX, CTX-M-1, TEM)	EC-2(NDM-5, OXA-1)
ATM	>256	0.25
ATM/AVI	16	0.25
ATM/VBR	128	0.25
CAZ	>256	>256
CAZ/AVI	>256	>256
MER	64	256
MER/VBR	128	>256

Figure 1a. EC-1

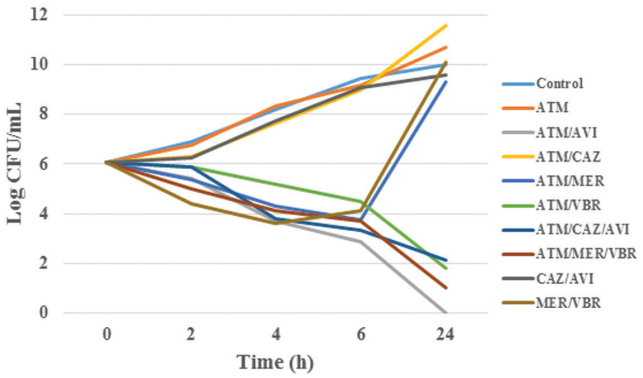
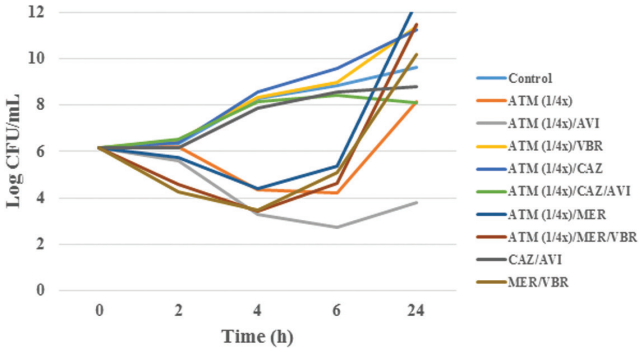


Figure 1b. EC-2



Disclosures. **E. Wenzler**, Melinta Therapeutics: Speaker's Bureau, Speaker honorarium.

2444. Incidence of Daptomycin Toxicity Among Patients With Vancomycin-Resistant *Enterococcus* Blood Stream Infections

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Background. Daptomycin (DAP) is a lipopeptide antibiotic and is first-line treatment for infections caused by Vancomycin-resistant *Enterococcus* (VRE). DAP is considered a safe antimicrobial agent, most commonly causing elevation of CPK. The historical incidence of DAP toxicity reported in the literature is low, ranging between 3 to 9%. We aim to describe the incidence of DAP toxicity among patients with VRE blood stream infection (BSI).

Methods. This is a retrospective cohort study conducted in a tertiary hospital in Cleveland, Ohio. We included all consecutive adult patients diagnosed with VRE BSI treated with DAP between November 2011 and January 2015. Patients were grouped based on dose of DAP received (Group 1: ≤6 mg/kg and Group 2 ≥ 8 mg/kg). Patient data were obtained from the microbiology department database, pharmacy information technology services and electronic medical records (EMR) (Table 1).

Results. During the study period, a total of 217 patients with VRE BSI were treated with DAP. (Table 1) The number of patients that received DAP dose of ≤6 mg/kg was 192 (88%), compared with 25 patients that received a DAP dose of ≥8 mg/kg (12%). The total incidence of DAP toxicity was present in only 3 patients (1.4%); and of those, only 2 patients developed CPK elevation leading to rhabdomyolysis requiring discontinuation of DAP (Maximum CPK value was 3142 U/L and 987 U/L for each case). The other patient developed a rash thought to be secondary to DAP. Of note, all 3 patients that developed DAP toxicity, received doses of ≤6 mg/kg.

Conclusion. In this retrospective cohort study of patients with VRE BSI treated with DAP, the incidence of DAP toxicity was only 3 cases out of 217 patients. All of these patients received doses of ≤6 mg/kg of DAP. This is lower than what is reported in the literature. DAP was well tolerated and the development of side effects did not seem to be related to the dose.