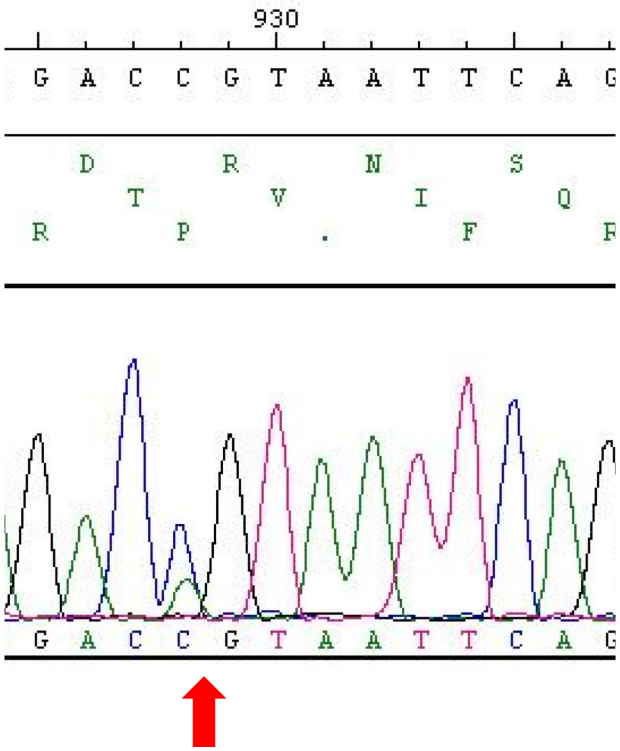
Figure 3: Sanger sequencing of *E. coli* 3p7



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

610. Meropenem-vaborbactam (MV) *In Vitro* Activity Against Carbapenem-Resistant *Klebsiella pneumoniae* (CRKP) Isolates with Outer Membrane Porin Gene Mutations

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Background. Vaborbactam is a cyclic boronic acid β-lactamase inhibitor (BLI) developed to potently inhibit Ambler class A&C enzymes, including KPC carbapenemases. Metallo-β-lactamases (MBL) and some Class D oxacillinases (OXA) are not inactivated by vaborbactam. Meropenem-vaborbactam (MV) was recently approved for the treatment of carbapenem-resistant Enterobacteriaceae complicated urinary tract infections. Recent studies have identified outer membrane porin (Ompk35 and -36) mutations in *Klebsiella pneumoniae* (KP) as a mechanism of decreased susceptibility to MV. We evaluated the activity of MV against a historical cohort of *KP* clinical isolates with these porin gene mutations.

Methods. WGS of carbapenem-resistant *KP* clinical isolates was performed and those harboring mutations in Ompk35 or Ompk36 were selected for testing. Strain *KP* ATCC BAA-1705 was used as a positive control. Meropenem and MV minimum inhibitory concentrations (MIC) were determined by broth microdilution (BMD) in custom 96-well plates (ThermoFisher Scientific) with a constant 8 μg/mL vaborbactam concentration. The MIC of ceftazidime–avibactam (CZA) was determined by standard BMD reference methods and interpreted according to CLSI criteria.

Results. A total of 105 *KP* isolates with either partial or complete mutations in outer membrane porin genes were included in the analysis. All isolates were resistant to Meropenem. The median MV MIC was 0.03 μg/mL (range, 0.015 to >16 μg/mL). Eleven isolates (10.4%) were resistant to MV. Sixteen additional isolates (16.1%) demonstrated higher than expected MV MICs ranging from 1 to 4 μg/mL. Only 1/11 resistant isolates harbored a gene for MBL production. Gene mutations in bla_{KPC} were not detected. See Table 1 for characteristics of resistant isolates.

Conclusion. Resistance and decreased susceptibility to MV is demonstrated in a historical cohort of *KP* clinical isolates dating back to 2013. WGS reliably identifies porin variants secondary to gene mutations in Ompk35 and Ompk36 as the underlying mechanism of decreased susceptibility. CZA appears to retain activity against these isolates. Caution should be exercised regarding the empiric use of MV against increasingly resistant *KP* as a result of non-β-lactamase-mediated mechanisms.

Table 1. Whole genome sequencing and MICs of MV resistant isolates

		MIC (μg/ml)			Typing	Enzymes	Outer membrane porin variant	
Strain	Date	MV	MEM	CZA	MLST	β-lactamase	OmpK35	OmpK36
1	2012	>16/8	>8	2/4	ST-258	KPC-2; SHV-160	FS 121insG	ins Gly134-Asp135
2	2015	>16/8	>8	2/4	ST-258	KPC-2; SHV-160	FS 121insG	WT
3	2017	>16/8	>8	>64	ST-147	NDM-5; OXA-181; CTXM-15; SHV-11	Partial FS	ins Asp135, Thr136
4	2014	16/8	>8	1/4	ST258	KPC-2; SHV-160	FS 121insG	ins Gly134-Asp135
5	2013	16/8	>8	1/4	ST-258	KPC-2, SHV-160	FS 121insG	ins Gly134-Asp135
6	2014	4/8	>8	1/4	ST-258	KPC-2; SHV-160	FS 121insG	ins Gly134-Asp135
7	2013	16/8	>8	1/4	ST-258	KPC-2, SHV-11	FS 121insG	ins Gly134-Asp135
8	2013	>16/8	>8	0.5/4	ST-258	KPC-2; SHV-160	FS 121insG	WT
9	2013	8/8	>8	1/4	ST-258	KPC-2, SHV-160	FS 121insG	ins Gly134-Asp135
10	2013	8/8	>8	4/4	ST-258	KPC-2; SHV-160	FS 121insG	ins Gly134-Asp135
11	2017	>16/8	>8	8/4	ST-258	KPC-2; SHV-11; SHV-12	FS stop aa89	ins Gly134-Asp135

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

611. Fosfomycin Resistance of Multidrug-Resistant *Escherichia coli* and Mechanisms of Fosfomycin Resistance

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Background. Fosfomycin is one of the antibiotics that may be a candidate for the next-generation antimicrobial agents againt multidrug-resistant bacteria. To date, it is known that the resistance rate is not high for *Escherichia coli*. However, it is necessary to update the fosfomycin resistance rates in *E. coli* according to the studies that extended spectrum β-lactamase (ESBL) producing *E. coli* strains are highly resistance to fosfomycin. We evaluated the resistance rate of fosfomycin, the resistant mechanism of fosfomycin in *E. coli*, and the activity of fosfomycin against susceptible and resistant strains of *E. coli*.

Methods. A total of 283 clinical isolates was collected from patients with *Escherichia coli* species during the period of January 2018 to June 2018, in three tertiary hospitals of Republic of Korea. *In vitro* antimicrobial susceptibility tests were performed in all E. coli isolates using the broth microdilution method according to the Clinical and Laboratory Standard Institute (CLSI). Multilocus sequence typing (MLST) of the Oxford scheme was conducted to determine the genotypes of *E. coli* isolated. Fosfomycin genes were investigated for all fosfomycin-resistant *E. coli* strains.

Results. The overall resistance rate to fosfomycin was 10.2%, compared with 53.4%, 46.3%, 41.3%, 31.1%, 10.6%, 2.5%, and 2.1% for ciprofloxacin, cefixime, cefepime, piperacillin/tazobactam, colistin, ertapenem, and amikacin, respectively. The 29 fosfomycin-resistant isolates did not show a clonal pattern on the phylogenetic tree. *MurA* and *glp* genes were identified in all strains. *FosA3* were identified in two strains and *uhp* gene were identified in 4 strains. In time-kill curve studies, fosfomycin was more bactericidal than cefixime against all sensitive *E. coli* strain. Morever, fosfomycin was more bactericidal than piperacillin/tazobactam against ESBL-producing *E. coli* strain.

Conclusion. The resistant rate of fosfomycin to *E. coli* is still low. Fosfomycin was active against *E. coli* including ESBL producing strains.

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612. Molecular Mechanisms Leading to Ceftolozane–Tazobactam Resistance in Clinical Isolates of *Pseudomonas aeruginosa* from Five Latin American Countries

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