Table 1.

Total Number Patients		N=217	
Groups by DAP Dose		**Group 1** (≤6mg/kg)	**Group 2** (≥8mg/kg)
Number of patients		192 (88%)	25 (12%)
Mean Age		58	58
Sex:	Male	113 (58%)	15(60)
	Female	79 (41%)	10 (40%)
DAP Toxicity:	CPK Elevation	2	0
	Rash	1	0

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2445. Efficacy and Tolerability of Linezolid for Treatment of Infectious Spondylitis

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Background. Infectious spondylitis requires long-term antibiotic treatment for 6 weeks or more, and the use of intravenous antibiotics during this period causes social loss and costs due to hospitalization. Linezolid has high oral bioavailability and is not affected by changes in renal or hepatic function. We investigated the clinical and microbiological effects of linezolid in infectious spondylitis caused by β-lactam resistant Gram-positive bacteria.

Methods. Clinical data about patients who were diagnosed infectious spondylitis and treated with linezolid for more than 4 weeks were collected by electronic medical record retrospectively at 3 tertiary hospitals from 2006 to 2016. Clinical and microbiological success after treatment were determined using medical record or bacterial culture results identified in blood or tissue.

Results. Twenty Korean cases were treated with linezolid more than 4 weeks during the study period. Median duration of linezolid treatment was 40.5 days. Major causative organism was methicillin-resistant *Staphylococcus aureus* (n = 15), followed by methicillin-resistant coagulase-negative *Staphylococcus* (n = 3). In 10 of 20 patients treated with linezolid, antibiotics were changed for side effects or de-escalation of antibiotics. The most common reason for discontinuation of linezolid was thrombocytopenia (n = 6). Fourteen patients were cured, 4 failed and 2 cases of mortality occurred due to other causes than infectious spondylitis. Nine of 13 patients who were assessed as vancomycin treatment failure were cured. Cytopenia was most common drug adverse reaction, and severe cytopenia (grade II or more of NCI criteria) was 11.11% in neutropenia, 12.96% in anemia and 20.37% in thrombocytopenia.

Conclusion. Linezolid can be used as an effective antibiotic agent in patients with infectious spondylitis, especially when treatment failure of the first-line treatment is expected. Linezolid can be administered orally in outpatient clinic, reducing healthcare cost. Since cytopenia (especially thrombocytopenia) are common, a regular follow-up of complete blood cell count is needed.

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2446. Clinical Spectrum and Outcomes of Colistin-Resistant Carbapenem-Resistant Enterobacteriaceae

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Background. Colistin is considered as one of the last resort of antibiotics against carbapenem-resistant enterobacteriaceae. During the last decade, increased use of colistin or polymyxins due to the increasing prevalence of carbapenem-resistant Gram-negative bacteria has unfortunately led to the emergence of colistin-resistant strains. There are no defined antibiotic regimens for colistin-resistant strains which makes the treatment of these organisms extremely challenging. We therefore report the clinical spectrum and outcomes of infections due to colistin-resistant carbapenem-resistant *Enterobacteriaceae* (Co-CRE) as well as the factors associated with acquisition of co-CRE.

Methods. We conducted a retrospective cross-sectional study from January 2013 till December 2017 on patients admitted to a tertiary care hospital in Karachi, Pakistan. Statistical analysis was done using SPSS 19.

Results. Forty patients with Co-CRE were identified of which 29 (72.5%) were males. Median age was 54.5 years. The most common organism isolated was *Klebsiella* in 22 (55%) followed by *Providencia* in 5 (12.5%) patients. Most common source of infection was the lung in 12 (30%) followed by urine in 11 (27.5%) patients. Similarly, the most common cause of bacteremia was pneumonia followed by intra-abdominal infections (50% and 37.5% of bacteremia cases, respectively). Twenty-eight (70%) patients had prior cultures with multi-drug-resistant organisms and 36 (90%) had used antibiotics in the past. A quarter (10) patients had pan resistant co-CRE strains while of the remaining strains 66% were sensitive to Fosfomycin. All patients received Colistin-based regimen in combination with 2 or 3 of the following: carbapenem, Fosfomycin, Amikacin, co-triamoxazole, and tigecycline. Complete clinical cure was achieved in only 50% of patients whereas microbiological eradication was achieved in 75%. Higher PITT bacteremia score, solid-organ transplant, and acute kidney injury were associated with mortality in patients with co-CRE.

Conclusion. Infections with co-CRE was seen in patients with prior nosocomial exposures and led to poor outcomes, despite combination treatment guided by susceptibilities.

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2447. Ertapenem and Faropenem for the Treatment of Drug-Resistant Tuberculosis

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Background. Carbapenems are a class of β-lactam antibiotics which include imipenem, meropenem and ertapenem. More recently, a new oral carbapenem (faropenem) have been marketed in a limited number of countries (in particular, India and Japan). Emerging evidence demonstrates that they target the mycobacterial cell wall, providing an alternative treatment for multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB), where options are limited. Compared with imipenem and meropenem (both only available as intravenous formulations), ertapenem (once daily administration) and faropenem (oral) are much more attractive alternatives for ambulatory or homecare treatment. However, there is a paucity of data on their efficacy against *M. tuberculosis*. The aim of this project was to test the *in vitro* activity of ertapenem and faropenem (with and without the addition of amoxicillin/clavulanate) against different clinical isolates of *M. tuberculosis* and the reference strain H37RV, to better understand their potential role as additional antibiotics in the management of drug-resistant TB.

Methods. Twenty isolates in total (19 clinical isolates, including MDR and XDR strains, plus H37Rv) were tested against different concentrations of ertapenem and faropenem (with and without the addition of amoxicillin/clavulanate). Susceptibility testing was performed using two different methods (BACTEC960 and broth microdilution). A degradation assay was also performed to evaluate the stability of ertapenem.

Results. Eighteen out of 20 samples were resistant to the highest concentration of ertapenem tested (including the addition of amoxicillin/clavulanate). Half of the samples tested showed some degree of susceptibility to faropenem and the addition of amoxicillin/clavulanate further reduced the MIC level in seven isolates.

Conclusion. The results from this project have highlighted a significant level of *in vitro* resistance to ertapenem, whilst the clinical isolates have shown different degrees of susceptibility to faropenem. Although promising agents (in particular, faropenem), carbapenems will remain a third line choice to be used only in cases of XDR TB. There is currently no evidence to prefer the use of ertapenem despite its once daily administration.

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2448. *In vitro* Activity of Ceftazidime–Avibactam Against *Enterobacteriaceae* Causing Intra-abdominal, Urinary Tract and Lower Respiratory Tract Infections Collected in Latin America as Part of the INFORM Global Surveillance Program, 2012–2016

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Background. The dissemination of multi-drug-resistant *Enterobacteriaceae* (MDR *Eba*) threatens the treatment of Gram-negative infections. Ceftazidime–avibactam (CAZ-AVI) is a novel antimicrobial with activity against *Eba* producing Class A, C and some Class D β-lactamases. This study evaluates the *in vitro* activity of CAZ-AVI against *Eba* isolates from urinary tract infections (UTI), intra-abdominal infections (IAI) and lower respiratory tract infections (LRTI) gathered in Latin America (LA) from 2012 to 2016.

Methods. A total of 7,037 non-duplicate *Eba* were collected from UTI, IAI, or LRTI in 26 sites in 6 countries in LA, as a part of the INFORM surveillance study from 2012 to 2016. Susceptibility testing was by broth microdilution using CLSI 2018 breakpoints. CAZ-AVI was tested with a fixed concentration of 4 μg/mL avibactam. Meropenem nonsusceptibility prompted β-lactamase screening by PCR and sequencing.

Results. CAZ-AVI demonstrated potent *in vitro* activity against *Eba* from UTIs, IAIs and LRTIs (99.6%, 99.8%, and 99.5% susceptible, respectively). CAZ-AVI was active against colistin-resistant and MDR *Eba* as well as meropenem-non-susceptible *Eba* not encoding metallo-β-lactamases (96.5%, 98.4% and 99.4% susceptible, respectively) (table).

	CAZ-AVI (%Susceptible, *n*)			
Phenotype	All (*n*)	UTI (*n*)	IAI (*n*)	LRTI (*n*)
Eba, All	99.6% (7,037)	99.6% (2,918)	99.8% (2,401)	99.5% (1,718)
CAZ-NS	98.7% (2,110)	98.4% (797)	99.2% (709)	98.5% (604)
MEM-NS	93.8% (372)	93.2% (147)	95.7% (116)	92.7% (109)
MEM-NS, MBL-negative	99.4% (351)	99.3% (138)	99.1% (112)	100% (101)
CST-R[a]	96.5% (144)	98.4% (63)	97.3% (37)	93.2% (44)
MDR[b]	98.4% (1,456)	98.1% (591)	98.8% (480)	98.2% (385)

Infection source: UTI, urinary tract; IAI, intra-abdominal tract; LRTI, lower respiratory tract. CAZ-AVI, ceftazidime–avibactam; CAZ, ceftazidime; MEM, meropenem; CST, colistin; MDR, multidrug-resistant; MBL, metallo-β-lactamase; NS, non-susceptible; R, resistant.

[a]Excludes Proteeae and *Serratia* spp; CST breakpoints are by EUCAST 2018.

[b]MDR, resistant to agents from ≥3 classes.

Conclusion. CAZ-AVI exhibited potent *in vitro* activity against *Eba* from UTIs, IAIs and LRTIs isolated in Latin America from 2012 to 2016 and provides a vital alternative to colistin and meropenem when MBLs are not present.

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2449. Validation of *In Vitro* Activity of Aminoglycosides Against Recently Isolated *Helicobacter pylori* for Commercialization of Gentamicin-Intercalated Smectite Hybrid as a New Therapeutic Agent

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Background. The eradication rate of *Helicobacter pylori* as a standard therapy based on amoxicillin and clarithromycin, exhibits a decreasing trend. Alternative approaches have been explored, but there is still controversy in the regimen change and these do not provide a satisfactory substitute to the existing standard therapy. Thus, a novel and efficient *H. pylori* eradication regimen should be developed. Smectite can serve as a drug delivery system and gentamicin-intercalated smectite hybrids (S-GEN) are expected to supersede the standard therapy for *H. pylori* eradication. In the previous study, we synthesized S-GEN complexes as a novel therapeutic agent. In a murine model, S-GEN released gentamicin to the gastric wall stably and the therapeutic effect was not inferior to the conventional standard therapy. The aim of this study was to confirm whether the minimum inhibitory concentration (MIC) of aminoglycosides applied as smectite hybrids remained low against recently isolated *H. pylori* strains.

Methods. The *H. pylori* strains were collected via endoscopic biopsy from 1,422 patients at Gangnam Severance Hospital in Seoul, Korea, between March 2015 and February 2018. Antimicrobial susceptibility tests were performed, and the MICs of eight antibiotics (amoxicillin, clarithromycin, metronidazole, tetracycline, levofloxacin, gentamicin, netilmicin, and tobramycin) were determined by using the Epsilometer test and following the European Committee on Antimicrobial Susceptibility Testing recommendations.

Results. Finally, 140 *H. pylori* strains were analyzed in this study. The resistance rate to clarithromycin was 30.7%, although it is a major antimicrobial agent used in standard therapy. The MIC_{50} and MIC_{90} of gentamicin (MIC_{50} 0.25 mg/L, MIC_{90} 0.75 mg/L) and netilmicin (MIC_{50} 0.19 mg/L, MIC_{90} 0.75 mg/L) were lower than that of metronidazole, tetracycline and levofloxacin, which are alternative therapies for *H. pylori* eradication. In clarithromycin-resistant strains, the MIC_{50} was 0.25 mg/L and the MIC_{90} was 1 mg/L for gentamicin; for netilmicin, the values were 0.25 mg/L and 0.75 mg/L, respectively.

Conclusion. Through the use of gentamicin and netilmicin, which have low MICs for *H. pylori*, aminoglycoside-intercalated smectite hybrids are expected to emerge as a new standard therapy for *H. pylori* eradication.

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2450. Antibiotic Treatment for Carbapenem-Resistant Enterobacteriaceae (CRE) and Outcomes in Veterans With Spinal Cord Injury/Disorder (SCI/D)

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Background. A total of 282,000 people (17% veterans) in the United States have SCI/D. Infection is a significant source of morbidity and the leading cause of death in this population. Due to frequent healthcare contact and antibiotic use, SCI/D is associated with high risk of multidrug-resistant infections, including CRE. CRE are resistant to most antibiotics and associated with high mortality. The objective of this study was to describe antibiotics used for CRE infection and clinical outcomes in veterans with SCI/D.

Methods. This retrospective cohort used national VA data of veterans with SCI/D and active CRE infection (per documentation in the health record) from 2011 to 2013. CRE was defined as resistant to a carbapenem and third-generation cephalosporin. Antibiotics were described by empiric/definitive and monotherapy/combination therapy. Clinical outcomes included clinical failure/improvement, microbiological resolution, mortality and readmission in 30 days/1 year. SAS was used for analysis with significance at $P \leq 0.0125$ due to multiple comparisons.

Results. Ninety-two CRE infections (62% *K. pneumoniae*) were identified in 87 patients, most often in urine cultures (58.7%). Carbapenems (20.7%) were used most frequently for CRE treatment. Combination therapy was used more often than monotherapy (empiric 56.3%, definitive 69.0%). Definitive combinations consisted of carbapenems/polymyxins (16.7%) or carbapenems/aminoglycosides (13.3%). Clinical outcomes for definitive monotherapy vs. combination, respectively, were: clinical failure (29.6% vs. 46.7%), improvement 1–10 days (48.2% vs. 33.3%), and 11–30 days (70.4% vs. 53.3%); microbiological resolution (48.2% vs. 38.3%); mortality at 30 days (22.2% vs. 30%), 90 days (22.2% vs. 41.7%), 1 year (25.9% vs. 51.7%) and readmission at 30 days (11.1% vs. 10%) and 1 year (37% vs. 30%). No significant differences in outcomes were identified for monotherapy vs. combination therapy or susceptible vs. nonsusceptible treatment.

Conclusion. For CRE treatment in the SCI/D population, carbapenems were the most widely used drug class; combination therapy was used most frequently. No improvements in clinical outcomes were found for combination therapy as either empiric or definitive treatment or for susceptible vs. nonsusceptible treatment.

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2451. Synergistic Activity of Ceftazidime–Avibactam in Combination With Polymyxin B Against Carbapenem-Resistant *Klebsiella pneumoniae*

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Background. Combination antimicrobial therapy is often recommended for the treatment of serious infections due to carbapenem-resistant *Klebsiella pneumoniae* (CRKP). Demonstrating synergy between ceftazidime–avibactam (C-A) and other antimicrobials *in vitro* may help elucidate the rate, magnitude, and duration of bactericidal activity and suggest combinations that may be effective in the clinical arena.

Methods. Three clinical CRKP were used for all experiments. C-A and polymyxin B (PB) MICs and time-kill analyses were performed in triplicate according to CLSI guidelines. Individual drugs were tested at ¼, ½, 1, 2, 4x MIC. A ≥3 $\log_{10}$ CFU/mL reduction compared with the starting inoculum (10^6) was considered bactericidal. Synergy was assessed by testing combinations at the highest concentration of each drug that showed no activity alone and was defined as ≥2 $\log_{10}$ CFU/mL increase in killing at 24 hours with the combination compared with most active agent alone.

Results. MICs: C-A 1, 8, 16 mg/L; PB 0.25, 0.25, 64 mg/L. C-A alone was bactericidal against all strains at 4× MIC (mean 24 hours bacterial reduction of 3.42 $\log_{10}$ CFU/mL). PB at 4× MIC was bactericidal for all strains at 6 hours (mean bacterial reduction of 3.58 $\log_{10}$ CFU/mL) but regrowth to control levels was seen at 24 hours. C-A alone at ½× MIC and combinations at ½× MIC for strains KPC1 and KPC2 yielded minimal killing followed by regrowth (mean 24 hours total bacterial count of 8.77 $\log_{10}$ CFU/mL). In contrast, bactericidal activity was observed at 24h with C-A alone at ½× MIC and in combination at ½× MIC (3.14 and 3.62 $\log_{10}$ CFU/mL reduction, respectively) for strain KPC3. Synergy was not observed for any isolate at the concentrations tested.

Conclusion. C-A demonstrated concentration-dependent bactericidal activity against all CRKP whereas PB showed initial bactericidality followed by regrowth and development of resistance. The combination of C-A and PB was not synergistic against C-A and PB susceptible or resistant CRKP isolates. Our data do not support the use of ceftazidime–avibactam in combination with polymyxin B for CRKP.