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 mini-dilution 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-nonsusceptible Eba not encoding metallo-β-lactamases (96.5%, 98.4% and 99.4% susceptible, respectively) (table).

| Phenotype | All | UTI (r) | IAI (r) | LRTI (r) |
|-----------|-----|---------|---------|---------|
| Eba, All  | 99.6% (1,327) | 99.8% (2,918) | 99.8% (2,401) | 99.5% (1,718) |
| CAZ-AVI   | 98.7% (2,110) | 98.4% (779) | 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% (122) | 100% (101) |
| CST-R(+)  | 96.5% (144) | 98.4% (63) | 97.3% (37) | 93.2% (44) |
| MDR(+)    | 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.

Conclusions. 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 Pharmacocleralization of Gentamicin-Intercalated Smectite Hybrid as a New Therapeutic Agent

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Session: 250. Treatment of AMR Infections Saturday, October 6, 2018: 12:30 PM

Background. The eradication rate of Helicobacter pylori as a standard therapy based on amoxicillin based on a previous study, exhibits a decreasing trend. Alternative approaches have been explored, but there is still controversy in the regimen change and recommendations. Individual drugs were tested at ¼, ½, 1, 2, 4x MIC. A combination of C-A and PB was not synergistic against recently isolated H. pylori strains.

Methods. Three clinical CRKP were used for all experiments. C-A and polymyxin B (MB) 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 23 log CFU/mL reduction compared with the starting inoculum (107) was considered bactericidal.

Results. Three clinical CRKP were used for all experiments. C-A and polymyxin B (MB) 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 23 log CFU/mL reduction compared with the starting inoculum (107) was considered bactericidal.

Conclusions. C-A and polymyxin B (MB) 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 23 log CFU/mL reduction compared with the starting inoculum (107) was considered bactericidal.

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2451. Synergistic Activity of Ceftazidime-Ampicillin 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 clinically significant infections due to carbapenem-resistant Klebsiella pneumoniae (CRKP). Demonstrating synergy between ceftazidime-ampicillin (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 (MB) 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 23 log CFU/mL reduction compared with the starting inoculum (107) was considered bactericidal.

Results. Three clinical CRKP were used for all experiments. C-A and polymyxin B (MB) 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 23 log CFU/mL reduction compared with the starting inoculum (107) was considered bactericidal.

Conclusions. C-A demonstrated concentration-dependent bactericidal activity against all CRKP whereas PB showed initial bactericidal 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-ampicillin in combination with polymyxin B for CRKP.
2452. Treatment and Outcomes of Daptomycin-Nonsusceptible Methicillin-Resistant Staphylococcus aureus Bloodstream Infections

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Background. Daptomycin (dap) is approved as an alternative to vancomycin (van) for therapy of methicillin-resistant Staphylococcus aureus (MRSA) bloodstream infection (BSI). Cases of therapy failure associated with the emergence of daptomycin-nonsusceptible (DNS) MRSA strains have been documented. Information on the treatment and outcome of DNS MRSA BSI is scarce. This study describes the treatment and outcome of patients with DNS MRSA BSI at our healthcare center.

Methods. This is a retrospective review of patients with DNS (E-test MIC >1 µg/mL) MRSA BSI at a tertiary healthcare center in Detroit, Michigan between September 24, 2005 and March 31, 2018. The variables collected were: BSI source, inpatient and discharge antibiotic therapy; BSI duration, in-hospital and 90-day mortality, and 90-day MRSA BSI recurrence. Inpatient therapy was defined as the treatment used for the most consecutive days from index DNS MRSA blood culture during hospitalization. Discharge therapy is the treatment used post-discharge or on the expiration date. Antibiotics used for ≥2 days were excluded.

Results. A total of 32 nonduplicate patients with DNS MRSA BSI were identified. One patient with an inaccessible chart was excluded. The source of BSI was endovascular in 9 (29%) patients, secondary BSI in 14 (45%), central-line associated in 5 (16%). A total of 24 different antibiotic regimens were used to treat DNS MRSA BSI. Van monotherapy was the most commonly used regimen for inpatient and discharge therapy; followed by dap + ceftaroline (cef). Table 1 is a summary of the results.

Table 1: Treatment and Outcomes of Patients with DNS MRSA BSI

| Inpatient Therapy | Discharge Therapy | In-Hospital | 90-Day Mean | 90-Day BSI |
|-------------------|-------------------|-------------|-------------|------------|
| Therapy (n)       | Therapy (n)       | Mortality, n (%) | Mortality, n (%) | Duration (days) | Recurrence, n (%) |
| van (10)           | van (8)           | 3(30)       | 4(40)       | 2.9        | 3(30)*       |
| dip + cef (5)      | dip + cef (11)    | 0(0)        | 0(0)*       | 4.4        | 12(10)**     |
| cef + dip (3)      | cef + dip (3)     | 1(20)       | 3(60)       | 6.8        | 1(20)        |
| van (1)           | van (1)          |             |             |            |             |
| lin + gen x       | lin (3) + van (1) | 4(36)       | 4(36)       | 3.5        | 2(20)*       |
| rif (5)           | rif (5)          | 1(20)       | 5(20)       | 1(20)      |             |
| sxt (1) + quin (1) | sxt (1) + quin (1)|             |             |            |             |
| dal (1)           | dal (1)          |             |             |            |             |
| other (11)        | other (11)       |             |             |            |             |

gen = gentamicin; rif = rifampin; lin = linezolid; sxt = TMP-SMX; quin/dal = quinupristin/dalfopristin.

*1 pt with unknown status.
**1 pt with unknown status.

Conclusion. A variety of therapeutic regimens was used to treat DNS MRSA BSI in our cohort. However, van monotherapy was the most common inpatient and discharge regimen.

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2453. Repeated Exposures to Minocycline/Rifampin and + Chlorhexidine Combination Used to Coat Catheters Fails to Induce Antimicrobial Resistance

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Background. Central venous catheters (CVC) impregnated with minocycline and rifampin (M/R) are recommended for use in high-risk patients to reduce catheter related bloodstream infections (CRBSI). We developed a second generation antimicrobial CVC with addition of chlorhexidine (CHD) for extended spectrum activity against virulent Gram-positive and Gram-negative bacteria as well. In Gramily we examined the potential for induced resistance with repeated exposure to M/R+CHD.

Methods. Potential to induce resistance was evaluated by exposing a broad-spectrum of CRBSI pathogens to serial passages of sub-inhibitory concentrations of M/R+CHD. Excluding MICs following each passage. Susceptibility to individual agents in the combination were assessed, to identify organisms that were originally resistant to the individual agents in the combination. A total of 24 Gram-positive, Gram-negative, and yeast pathogens were evaluated for baseline MICs following standard CLSI procedures. Subsequently, organisms that were exposed to one half the MIC were cultured and MICs retested. This process was carried out for a total of 21 passages to assess trends in MICs and potential for induction of resistance. Any organism with ≥4 fold increase in MIC were then passed in broth alone to assess phenotypic adaptation.

Results. Synergy in the triple combination of M/R + CHD was detected for several resistant organisms that had low susceptibilities to the individual components but were highly susceptible to the combination. After a series of 21 passages, the organisms maintained the same MIC values as baseline with no clinically significant increases. One strain of Enterobacter showed a 4-fold MIC increase; however, the MIC returned to baseline after culturing in broth alone.

Conclusion. Repeated exposure of M/R + CHD failed to show induced anti-microbial resistance among a large number of pathogens with both low and high susceptibilities. Furthermore, any increase in MIC to return with the removal of the combined M/R + CHD, indicating that the increase in MIC was a phenotypic adaptation rather than induced resistance. Surveillance studies assessing development of resistance will need to be conducted in a clinical setting.

Disclosures. 1. Raad, The University of Texas MD Anderson Cancer Center: Shareholder, Licensing agreement or royalty. 2. The University of Texas MD Anderson Cancer Center: Shareholder, Dr. Raad is a co-inventor of the Nitroglucerin-Citrate-Ethanol catheter lock solution technology which is owned by the University of Texas MD Anderson Cancer Center (UTMDACC) and has been licensed to Novel Anti-Infective Technologies LLC, in which UTMDACC and Licensing agreement or royalty.

2454. Pertussis Vaccine Effectiveness and Waning Immunity in Alberta, Canada: 2004–2015

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Background. Despite childhood vaccination coverage rates exceeding 75%, pertussis is still frequently reported in Canada. In Alberta, pertussis incidence ranged from 1 to 2.5 cases per 100,000 persons for 2004–2015. Most cases occurred in those aged <15 years. We investigated pertussis vaccine effectiveness (VE) using a test-negative designed (TND) study.

Methods. All individuals who had undergone a real-time PCR laboratory test for Bordetella pertussis between January 1, 2004 and August 31, 2015, in the province of Alberta, Canada were included. Vaccination history was obtained from Alberta’s immunization repository. Vaccination status was classified as complete, incomplete, or not vaccinated, based on the province’s vaccination schedule. Multivariable logistic regression models were used to estimate adjusted odds ratios (aOR) and 95% confidence intervals (95% CI) for pertussis infection by time since last vaccination, comparing those with complete or incomplete vaccination to those not vaccinated. We adjusted for age, sex, income, urban/rural status, and the presence of a co-morbid condition. Vaccine effectiveness (VE) was calculated as [(1-aOR)×100].

Results. Of 28,154 individuals tested, 2.297 (12.3%) were positive for B. pertussis. Among those with complete vs. no vaccination, VE was 88% (95% CI 85–91%) at 1 year, 83% (95% CI 79–86%) at 1 to 3 years, 70% (95% CI 63–76%) at 4 to 6 years, 28% (95% CI 12–42%) at 7 to 9 years, and 4% (95% CI 53–29%) at 10 or more years since a last dose of a pertussis vaccine (Figure 1). VE was similar but attenuated in the incompletely vaccinated group, with a comparable waning of immunity.

Conclusion. Pertussis VE was high in the first year after vaccination, then declined noticeably after 5 years. Our results suggest there is a large number of adolescents and adults susceptible to pertussis. Regular boosters through childhood and adolescence, and during pregnancy are critical to protect those at greatest risk of infection and complications. Further validation of the strengths and weaknesses of the TND for assessing pertussis VE is needed.