in conjunction with UTI symptoms from 1/2018-12/2020. Individual UTI events were excluded if associated with potential sources of harbored infection, anatomic abnormalities increasing risk of bacteriuria, non-bacterial pathogens, concurrent infections prolonging antibiotic treatment, or antibiotic courses managed outside of VASDHS. Treatment groups comprised UTI events treated with no more than 7 days of antibiotics (group 1) versus more than 7 days (group 2). Study endpoints were recurrence or new incidence of UTI within 30 and 90 days after completion of antibiotic treatment and onset of *C. difficile* infection or death within 30 or 90 days, respectively, after treatment completion. Statistical tests included Chi-square, Mann-Whitney U, and logistic regression.

Results. One-hundred and seven patients with 241 unique UTI events were included in this study, with 79 events in group 1 and 162 events in group 2. Baseline characteristics were similar across both groups, aside from a higher incidence of hospital admission and more severe SCI/D based on the American Spinal Cord Injury Association (ASIA) impairment scale in group 2. Efficacy outcomes are described in Table 1. No deaths occurred within 90 days of treatment completion, and *C. difficile* infection occurred in 1 patient in group 2 after 3 days of antibiotic therapy. Duration of antibiotic therapy was not predictive of treatment failure within 30 days of antibiotic completion. Factors predictive of treatment with longer courses of antibiotic therapy included hospital admission and more severe ASIA impairment scale score.

Table 1. Incidence of UTI after antibiotic completion

Outcome – n (%)	*Group 1 (n=79)*	*Group 2 (n=162)*	*P-value*	*OR (95% CI)*
UTI within 30 days	7 (8.9)	24 (14.8)	0.195	1.789 (0.735-4.351)
Recurrent UTI	6 (7.6)	14 (8.6)	0.782	1.151 (0.425-3.118)
New UTI	1 (1.3)	10 (6.2)	0.087	5.132 (0.645-40.817)
UTI within 90 days	15 (19.0)	45 (27.8)	0.138	1.641 (0.849-3.172)
Recurrent UTI	9 (11.4)	27 (16.7)	0.281	1.556 (0.694-3.489)
New UTI	6 (7.6)	18 (11.1)	0.392	1.521 (0.579-3.995)

Conclusion. The findings of this study suggest that for some patients with SCI/D, UTI treatment lasting 7 days or fewer may be effective compared to longer courses of antibiotics and could be beneficial in reducing collateral damage from antibiotic use.

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

199. Polymorphisms in Key Regulatory Regions of the *bla* operon Correlate with the Cefazolin Inoculum Effect in Methicillin-Susceptible *Staphylococcus aureus* (MSSA)

Sara I. Gomez-Villegas, MD[1]; Rafael Rios, MSc[2]; Lorena Diaz, PhD [2]; Lorena Diaz, PhD [2]; An Q. Dinh, BS[3]; Diana Panesso, Ph.D. [4]; Sandra Rincon, PhD[5]; Lina P. Carvajal, PhD student [6]; Maria I. Reyes, n/a[7]; Barbara E. Murray, M.D.[3]; William R. Miller, MD [8]; William R. Miller, MD [8]; Kavindra V. Singh, Ph.D.[3]; Jinnethe Reyes, MSc, PhD[6]; Cesar A. Arias, M.D., MSc, Ph.D., FIDSA[9]; [1]University of Texas Health Sciences Center at houston, Houston, TX; [2]Universidad El Bosque, Bogota, Distrito Capital de Bogota, Colombia; [3]Center for Antimicrobial Resistance and Microbial Genomics, UTHealth, Houston, TX,, Houston, Texas; [4]McGovern Medical School, Houston, TX; [5]Universidad el Bosque, Bogota, Distrito Capital de Bogota, Colombia; [6]Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, Bogota, Colombia, Bogota, Distrito Capital de Bogota, Colombia; [7]UTHSC at Houston Mc Govern Medical School, Houston, Texas; [8]Center for Antimicrobial Resistance and Microbial Genomics, UTHealth, Houston, TX; [9]CARMiG, UTHealth and Center for Infectious Diseases, UTHealth School of Public Health, HOU, TX; Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, BOG, COL, Houston, Texas

Session: O-40. What's New in Antimicrobial Resistance

Background. The cefazolin inoculum effect (CzIE), defined as Cz minimum inhibitory concentration ≥ 16 µg/ml at high inoculum (HI-MIC), has been associated with poor clinical outcomes in patients with MSSA bacteremia or osteomyelitis. The CzIE is correlated with the presence of the *blaZ* gene, one of the components of the *bla* operon encoding the BlaZ β-lactamase (type A, B, C or D). Other portions of the *bla* operon include *blaR* and *blaI* (encoding the antibiotic sensor and transcriptional repressor, respectively) and the intergenic region with operator and promoter sequences (**Figure 1**). In BlaR, residue 293 mediates signal transduction, and the Z and R dyads in the intergenic region are the DNA-binding sites for BlaI (**Figure 2**). Previous experiments have shown that the regulatory portions of the *bla* operon play a key role in the CzIE. Here, we investigated the association between the CzIE and specific variations in the regulatory sequences of the *bla* operon.

Figure 1. Functioning of the bla operon and the production of the staphylococcal β-lactamase BlaZ.

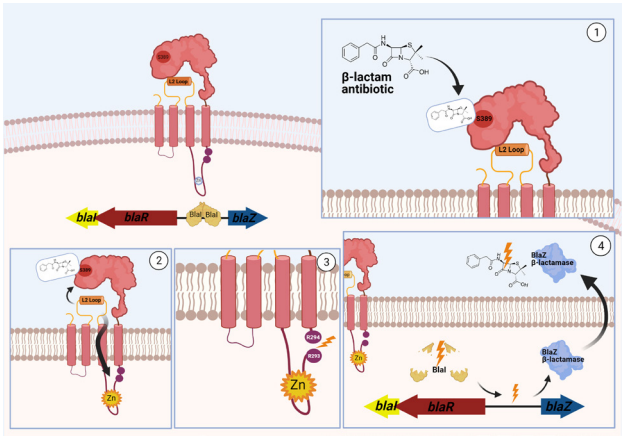
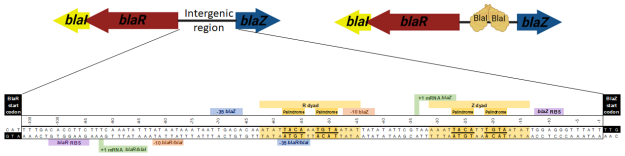


Figure 2. Structure and key regions of the intergenic region of the bla operon, including the promoter and the BlaI DNA-binding regions (Z and R dyads).



Methods. A total of 437 MSSA containing *blaZ* were evaluated for the CzIE using broth microdilution at high inoculum. Using whole genome sequencing, the sequences of the *bla* operons were classified into cassettes based on unique changes in predicted amino acid sequences of BlaZ, BlaR and BlaI paired with specific nucleotide alterations in the intergenic region. The *bla* operon sequence of *S. aureus* ATCC29213 was used as reference (cassette 0).

Results. Among 437 MSSA isolates, 46% exhibited the CzIE. We identified 55 unique *bla* cassettes. The *bla* cassettes were phylogenetically grouped in 7 clusters (**Figure 3**) which grouped cassettes with different BlaZ types and variations in the Z dyad, the -35 box, residue 293 of BlaR, and the *blaI* ribosomal binding site. Each cluster had an association to the CzIE and distinct Cz HI-MICs. The combination of: a BlaZ type A, C or D, an adenine in the position -66 of *blaZ* (-35 box of *blaZ*), a cytosine in the position -22 of *blaZ*(Z dyad), and either an arginine or a serine in position 293 of BlaR was a very strong predictor of the CzIE (**Figure 4**).

Figure 3. Phylogenetical organization of bla operon cassettes into clusters, their association with polymorphisms in key regulatory regions and the CzIE. GM Cz-MIC: Geometric mean of the Cefazolin MIC at high Inoculum.

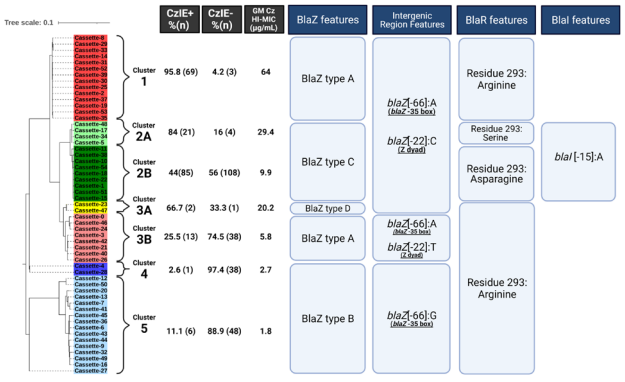
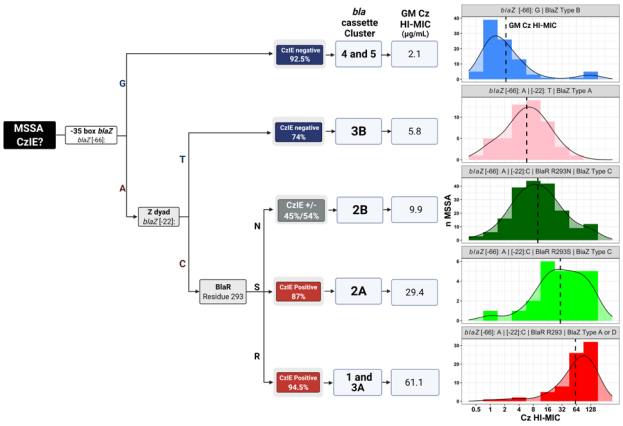


Figure 4. Variations of the bla operon, their association with the CzIE, their GM (Geometric Mean) of the Cefazolin MIC and the MIC distribution of the strains with each specific combination of polymorphisms.



Conclusion. Specific variations in regulatory portions of the *bla* operon, which are likely to influence BlaZ expression, are highly associated with the CzIE, supporting the notion that regulation of *blaZ* is the key factor responsible for the CzIE in MSSA.

Disclosures. **Lorena Diaz, PhD** , Nothing to disclose **William R. Miller, MD** , **Entasis Therapeutics** (Scientific Research Study Investigator)**Merck** (Grant/Research Support) **William R. Miller, MD** , Entasis (Individual(s) Involved: Self): Scientific Research Study Investigator; Merck (Individual(s) Involved: Self): Grant/Research Support **Cesar A. Arias, M.D., MSc, Ph.D., FIDSA**, **Entasis Therapeutics** (Grant/Research Support)**MeMed Diagnostics** (Grant/Research Support)**Merck** (Grant/Research Support)

200. Antimicrobial Activity of Ceftazidime-Avibactam and Comparators against AmpC Hyperproducing *Enterobacterales* and *P. aeruginosa* Collected from United States (US) Medical Centers (2016-2020)

Helio S. Sader, MD, PhD, FIDSA[1]; Cecilia G. Carvalhaes, MD, PhD[2]; Rodrigo E. Mendes, PhD[1]; Mariana Castanheira, PhD[1]; Mariana Castanheira, PhD[1]; [1]JMI Laboratories, North Liberty, Iowa; [2]JMI Laboratories, Inc., North Liberty, Iowa

Session: O-40. What's New in Antimicrobial Resistance

Background. *E. cloacae* species complex (ECL), *S. marcescens* (SM), *C. freundii* species complex (CF), and *P. aeruginosa* (PSA) are common pathogens in a variety of clinical infections. These organisms can overexpress the chromosomal AmpC that encodes resistance to several β-lactams. We evaluated the activity of ceftazidime-avibactam (CAZ-AVI) and comparators against these organisms.

Methods. 17,650 isolates, including 4,400 ECL, 2,074 SM, 1,644 CF, and 9,532 PSA, were consecutively collected from 88 US medical centers in 2016-2020. Among these isolates, 3,127 were ceftazidime-nonsusceptible (CAZ-NS; MIC ≥8 mg/L for *Enterobacterales* [ENT] and ≥16 mg/L for PSA) and considered probable AmpC hyperproducers. Isolates were susceptibility tested by broth microdilution method.

Results. Susceptibility to CAZ ranged from 73.6% (ECL) to 97.5% (SM; Table). Overall, 99.8% of ENT (99.7-99.9%) and 97.1% of PSA were CAZ-AVI-S; whereas 84.3% (79.0-97.7%) of ENT and 97.4% of PSA were ceftolozane-tazobactam (C-T)-S, 83.0% (78.5-94.8%) of ENT and 80.0% of PSA were piperacillin-tazobactam (PIP-TAZ)-S, and 98.4% (98.3-98.7%) of ENT and 79.5% of PSA were meropenem (MEM)-S. CAZ-AVI retained potent activity and broad spectrum against CAZ-NS ENT (n=1,629; $MIC_{50/90}$, 0.5/1 mg/L; 99.0%S overall) and CAZ-AVI was more active than MEM ($MIC_{50/90}$, 0.06/0.5 mg/L; 93.1%S) against these organisms. C-T ($MIC_{50/90}$, 8/ >16 mg/L; 23.8%S) and PIP-TAZ ($MIC_{50/90}$, 64/ >64 mg/L; 21.8%S) exhibited limited activity against CAZ-NS ENT. Among comparator agents, only amikacin (99.0%S), tigecycline (95.6%S), and imipenem (92.1%S) showed good activity against CAZ-NS ENT. Also, CAZ-AVI retained activity against 86.7% of ENT isolates that were NS to CAZ and MEM (n=113). CAZ-AVI ($MIC_{50/90}$, 2/4 mg/L; 97.1%S) and C-T ($MIC_{50/90}$, 0.5/2 mg/L; 97.4%S) were the most active compounds tested against PSA and both retained activity against CAZ-NS PSA. CAZ-AVI ($MIC_{50/90}$, 4/16 mg/L; 81.8%S) and C-T ($MIC_{50/90}$, 2/8 mg/L; 83.9%S) activity against CAZ-NS PSA was comparable to tobramycin ($MIC_{50/90}$, 1/ >8 mg/L; 82.2%S).

Conclusion. CAZ-AVI demonstrated potent activity and broad spectrum against AmpC hyperproducer organisms, such as ECL, SM, CF, and PSA, from US hospitals and remained highly active against CAZ-NS isolates.

	% Susceptible per CLSI and US FDA criteria								
Organisms	All isolates					Ceftazidime-non-susceptible			
(no. tested: all / CAZ-NS)	CAZ-AVI	C-T	PIP-TAZ	MEM	CAZ	CAZ-AVI	C-T	PIP-TAZ	MEM
Enterobacterales (8,118 / 1,629)	99.8	84.3	83.0	98.4	79.9	99.0	23.8	21.8	93.1
E. cloacae (4,400 / 1,162)	99.7	80.0	79.2	98.3	73.6	98.6	25.2	22.2	93.9
S. marcescens (2,074 / 52)	99.9	97.7	94.8	98.7	97.5	94.2	30.8	42.3	69.2
C. freundii (1,644 / 415)	99.9	79.0	78.5	98.4	74.8	99.8	19.2	18.1	93.7
P. aeruginosa (9,532/ 1,498)	97.1	97.4	80.0	79.5	84.3	81.8	83.9	5.8	41.7
All organisms (17,650 / 3,127)	98.4	91.3	81.4	88.2	82.3	90.7	52.2	14.1	68.4

Disclosures. **Helio S. Sader, MD, PhD, FIDSA**, **AbbVie (formerly Allergan)** (Research Grant or Support)**Basilea Pharmaceutica International, Ltd.** (Research Grant or Support)**Cipla Therapeutics** (Research Grant or Support)**Cipla USA Inc.** (Research Grant or Support)**Department of Health and Human Services** (Research Grant or Support, Contract no. HHSO100201600002C)**Melinta Therapeutics, LLC** (Research Grant or Support)**Nabriva Therapeutics** (Research Grant or Support)**Pfizer, Inc.** (Research Grant or Support)**Shionogi** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Cecilia G. Carvalhaes, MD, PhD**, **AbbVie (formerly Allergan)** (Research Grant or Support)**Cidara Therapeutics, Inc.** (Research Grant or Support)**Cipla Therapeutics** (Research Grant or Support)**Cipla USA Inc.** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Pfizer, Inc.** (Research Grant or Support) **Rodrigo E. Mendes, PhD**, **AbbVie** (Research Grant or Support)**AbbVie (formerly Allergan)** (Research Grant or Support)**Cipla Therapeutics** (Research Grant or Support)**Cipla USA Inc.** (Research Grant or Support)**ContraFect Corporation** (Research Grant or Support)**GlaxoSmithKline, LLC** (Research Grant or Support)**Melinta Therapeutics, Inc.** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Nabriva Therapeutics** (Research Grant or Support)**Pfizer, Inc.** (Research Grant or Support)**Shionogi** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Mariana Castanheira, PhD**, **AbbVie (formerly Allergan)** (Research Grant or Support)**Bravos Biosciences** (Research Grant or Support)**Cidara Therapeutics, Inc.** (Research Grant or Support)**Cipla Therapeutics** (Research Grant or Support)**Cipla USA Inc.** (Research Grant or Support)**GlaxoSmithKline** (Research Grant or Support)**Melinta Therapeutics, Inc.** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Pfizer, Inc.** (Research Grant or Support)**Qpex Biopharma** (Research Grant or Support)**Shionogi** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Mariana Castanheira, PhD**, Affinity Biosensors (Individual(s) Involved: Self): Research Grant or Support; Allergan (Individual(s) Involved: Self): Research Grant or Support; Amicrobe, Inc (Individual(s) Involved: Self): Research Grant or Support; Amplyx Pharma (Individual(s) Involved: Self): Research Grant or Support; Artugen Therapeutics USA, Inc. (Individual(s) Involved: Self): Research Grant or Support; Astellas (Individual(s) Involved: Self): Research Grant or Support; Basilea (Individual(s) Involved: Self): Research Grant or Support; Beth Israel Deaconess Medical Center (Individual(s) Involved: Self): Research Grant or Support; BIDMC (Individual(s) Involved: Self): Research Grant or Support; bioMerieux Inc. (Individual(s) Involved: Self): Research Grant or Support; BioVersys Ag (Individual(s) Involved: Self): Research Grant or Support; Bugworks (Individual(s) Involved: Self): Research Grant or Support; Cidara (Individual(s) Involved: Self): Research Grant or Support; Cipla (Individual(s) Involved: Self): Research Grant or Support; Contrafect (Individual(s) Involved: Self): Research Grant or Support; Cormedix (Individual(s) Involved: Self): Research Grant or Support; Crestone, Inc. (Individual(s) Involved: Self): Research Grant or Support; Curza (Individual(s) Involved: Self): Research Grant or Support; CXC7 (Individual(s) Involved: Self): Research Grant or Support; Entasis (Individual(s) Involved: Self): Research Grant or Support; Fedora Pharmaceutical (Individual(s) Involved: Self): Research Grant or Support; Fimbrion Therapeutics (Individual(s) Involved: Self): Research Grant or Support; Fox Chase (Individual(s) Involved: Self): Research Grant or Support; GlaxoSmithKline (Individual(s) Involved: Self): Research Grant or Support; Guardian Therapeutics (Individual(s) Involved: Self): Research Grant or Support; Hardy Diagnostics (Individual(s) Involved: Self): Research Grant or Support; IHMA (Individual(s) Involved: Self): Research Grant or Support; Janssen Research & Development (Individual(s) Involved: Self): Research Grant or Support; Johnson & Johnson (Individual(s) Involved: Self): Research Grant or Support; Kaleido Biosceinces (Individual(s) Involved: Self): Research Grant or Support; KBP Biosciences (Individual(s) Involved: Self): Research Grant or Support; Luminex (Individual(s) Involved: Self): Research Grant or Support; Matrivax (Individual(s) Involved: Self): Research Grant or Support; Mayo Clinic (Individual(s) Involved: Self): Research Grant or Support; Medpace (Individual(s) Involved: Self): Research Grant or Support; Meiji Seika Pharma Co., Ltd. (Individual(s) Involved: Self): Research Grant or Support; Melinta (Individual(s) Involved: Self): Research Grant or Support; Menarini (Individual(s) Involved: Self): Research Grant or Support; Merck (Individual(s) Involved: Self): Research Grant or Support; Meridian Bioscience Inc. (Individual(s) Involved: Self): Research Grant or Support; Micromyx (Individual(s) Involved: Self): Research Grant or Support; MicuRx (Individual(s) Involved: Self): Research Grant or Support; N8 Medical (Individual(s) Involved: Self): Research Grant or Support; Nabriva (Individual(s) Involved: Self): Research Grant or Support; National Institutes of Health (Individual(s) Involved: Self): Research Grant or Support; National University of Singapore (Individual(s) Involved: Self): Research Grant or Support; North Bristol NHS Trust (Individual(s) Involved: Self): Research Grant or Support; Novome Biotechnologies (Individual(s) Involved: Self): Research Grant or Support; Paratek (Individual(s) Involved: Self): Research Grant or Support; Pfizer (Individual(s) Involved: Self): Research Grant or Support; Prokaryotics Inc. (Individual(s) Involved: Self): Research Grant or Support; QPEX Biopharma (Individual(s) Involved: Self): Research Grant or Support; Rhode Island Hospital (Individual(s) Involved: Self): Research Grant or Support; RIHML (Individual(s) Involved: Self): Research Grant or Support; Roche (Individual(s) Involved: Self): Research Grant or Support; Roivant (Individual(s) Involved: Self): Research Grant or Support; Salvat (Individual(s) Involved: Self): Research Grant or Support; Scynexis (Individual(s) Involved: Self): Research Grant or Support; SeLux Diagnostics (Individual(s) Involved: Self): Research Grant or Support; Shionogi (Individual(s) Involved: Self): Research Grant or Support; Specific Diagnostics (Individual(s) Involved: Self): Research Grant or Support; Spero (Individual(s) Involved: Self): Research Grant or Support; SuperTrans Medical LT (Individual(s) Involved: Self): Research Grant or Support; T2 Biosystems (Individual(s) Involved: Self): Research Grant or Support; The University of Queensland (Individual(s) Involved: Self): Research Grant or Support; Thermo Fisher Scientific (Individual(s) Involved: Self): Research Grant or Support; Tufts