CLSI M100 MIC breakpoints. Clinically relevant, non-duplicate, isolates cultured from patients with SSSIs in 6 countries in LA in 2017 were tested by the AWARE Surveillance Program central laboratory (IHMA). In total, 1,435 non-duplicate isolates of MSSA, MRSA, β-hemolytic streptococci, and *Enterobacteriaceae* were tested: Argentina (*n* = 349/24.3% of all isolates tested), Brazil (114/7.9%), Chile (153/10.7%), Columbia (175/12.2%), Mexico (339/23.6%), and Venezuela (305/21.3%).

Results. CPT activity is summarized in the following table.

Bacteria	*n*	CPT MIC Breakpoints (µg/mL) S | I | R	CPT MIC (µg/mL) MIC_{50}	MIC_{90}	CPT MIC Interpretation % S	% I	% R
MSSA	354	≤1 | 2 | ≥4	0.25	0.5	100	0	0
MRSA	389	≤1 | 2 | ≥4	0.5	1	95.1	4.9	0
β-Hemolytic streptococci[a]	130	≤0.5 | – | –	0.008	0.015	100	–	–
Enterobacteriaceae, All	562	≤0.5 | 1 | ≥2	0.5	>128	55.3	3.9	40.8
Enterobacteriaceae, ESBL screen-negative	358	≤0.5 | 1 | ≥2	0.12	1	86.6	5.9	7.5

[a]*S. pyogenes* (*n* = 90), *S. agalactiae* (*n* = 26), and *S. dysgalactiae* (*n* = 14).

Conclusion. Overall, 100% of MSSA and 95.1% of MRSA from LA were susceptible to CPT (MIC ≤1 µg/mL); 19 isolates of MRSA were CPT-intermediate (MIC 2 µg/mL) with 17 of the 19 isolates being from Chile; no CPT-resistant MRSA were observed. All β-hemolytic streptococci and 86.6% of ESBL-negative *Enterobacteriaceae* were also susceptible to CPT. CPT continues to demonstrate potent *in vitro* activity against clinically relevant pathogens associated with SSSIs for patients in LA.

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2377. Outcomes in Patients With History of Cardiac or Vascular Disease (CV) During Treatment of Acute Bacterial Skin And Skin Structure Infection (ABSSSI) With Delafloxacin (DLX) vs. Vancomycin/Aztreonam (VAN/AZ)

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Background. DLX, an anionic fluoroquinolone antibiotic with Gram-positive and Gram-negative activity, was recently approved for treatment of ABSSSI. Two global phase 3 ABSSSI trials (studies 302 and 303) included patients with cardiac or vascular disease.

Methods. Two multicenter, double-blind, double-dummy trials of adults with ABSSSI patients randomized 1:1 to receive either DLX monotherapy or VAN 15 mg/kg (actual body weight) with AZ for 5–14 days. Study 302 used DLX 300 mg BID IV only; study 303 used DLX 300 mg BID IV for 3 days with a mandatory blinded switch to DLX 450 mg oral BID. Key endpoints were objective response at 48–72 hours with ≥20% reduction in lesion size; and Investigator assessment of outcome based on resolution of signs and symptoms at Follow-up (FU day 14) and Late Follow-up (LFU day 21–28).

Results. In the two studies, 488 CV patients were randomized in United States, Europe, Latin America and Asia. 57% were male with mean age 59 years. Average erythema area at baseline was 446 cm^2. 58% had cellulitis, 19% abscesses, 22% wound and 1% burns. Key endpoints are given in the following table.

	DLX, *n*/Total (%)	VAN/AZ, *n*/Total (%)
Objective response 48–72h (ITT)	208/260 (80.0%)	183/228 (80.3%)
Investigator-Assessed Success (FU CE)	204/217 (94.0%)	176/185 (95.1%)
Investigator-Assessed Success (LFU CE)	194/207 (93.7%)	173/182 (95.1%)
Micro Success (FU ME) for *S. aureus*	72/74 (97.3%)	57/61 (93.4%)

The % of CV patients with at least one treatment-related adverse event (AE) was similar for DLX (22.7%) compared with VAN/AZ (22.4%). There were 2 DLX and 5 VAN/AZ-treated CV patients discontinued due to related AEs. The most frequent treatment-related AEs were gastrointestinal including diarrhea seen in 8.2% and 3.1% of DLX and VAN/AZ patients respectively, generally mild to moderate in nature with no cases of *C. difficile* diarrhea. There were no cardiac events or deaths attributed to either study drug.

Conclusion. In CV patients, fixed dose DLX monotherapy was comparable to VAN/AZ in treatment of ABSSSI based on the early objective and investigator assessed responses at FU and LFU. DLX was also comparable to VAN/AZ in treating patients with *S. aureus*. There were no cardiac events or deaths in either study group. DLX appears effective and well tolerated in CV patients with ABSSSI.

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2378. Resolution of Signs and Symptoms (S&S) of Acute Bacterial Skin and Skin Structure Infections (ABSSSI) With Delafloxacin (DLX) IV/Oral Therapy

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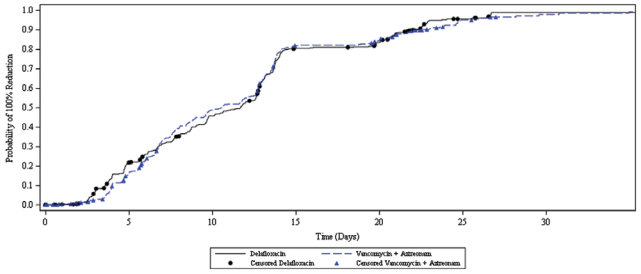
Background. Delafloxacin, a fluoroquinolone antibiotic with Gram-negative and Gram-positive activity including MRSA, was approved for treatment of ABSSSI. In a phase 3 ABSSSI trial, DLX was non-inferior to VAN/AZ in both objective and clinical response endpoints. Clinical signs and symptoms (S&S) and lesion size measurements also were evaluated in this trial.

Methods. A multicenter, double-blind trial of adults with ABSSSI patients randomized 1:1 to receive either DLX monotherapy 300mg q12h IV with switch to oral 450 mg q12h or vancomycin (VAN) 15 mg/kg (actual body weight) with aztreonam (AZ) for 5–14 days. AZ was discontinued once Gram-negative infection was excluded in the VAN arm. The presence or absence of clinical S&S were collected at each evaluation timepoint. Patients with complete resolution of S&S were classified as complete cures. Lesions were measured by digital planimetry. Patient-reported pain was recorded by numerical rating scale (NRS; 0=no pain, 10= worst pain). Assessments were completed at baseline, during and at end of treatment (EOT), at Follow-up (FU day 14) and Late Follow-up (LFU day 21–28).

Results. 850 patients were randomized in United States, Europe, Asia and Latin America. 63% were male with mean age 51 years. 48% had cellulitis, 25% abscesses, 26% wound and 1% burn infections. Baseline erythema and induration were reported in 100% and 93% of patients, respectively. Mean area of erythema and induration at baseline was 353 and 138 cm^2 respectively. Most common locations for lesions were lower extremities (56%) and upper extremities (24%). *S. aureus* was the most common isolate. Mean days of treatment was 7 days in either group. DLX and VAN/AZ patients had comparable impact on S&S with complete resolution in 42% vs. 45% at EOT, and 58% vs. 60% at FU, and 68% vs. 71% at LFU respectively. DLX was comparable to VAN/AZ in percent reduction in erythema over time (figure). There was a mean reduction of 58% vs. 53% at 48–72 h, 90% vs. 87% at EOT, and 98% vs. 97% at LFU for DLX and VAN/AZ respectively (figure). Baseline mean pain scores were 7/10 with scores of ~1/10 at EOT and ~0.5/10 at FU for both treatment groups.

Conclusion. Treatment with DLX and VAN/AZ provided equally rapid improvement in clinical signs and symptoms in ABSSSI with comparable reductions in S&S, lesion size and pain score.



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2379. Multicenter Evaluation of Ceftazidime–Avibactam for Multidrug-Resistant Gram-Negative Bacterial Infections

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Background. The increasing prevalence of multidrug-resistant (MDR) Gram-negative bacteria (GNB) represents an urgent public health threat. Ceftazidime–avibactam (CZA) is a novel cephalosporin/β-lactamase inhibitor with activity against MDR GNB including carbapenem-resistant Enterobacteriaceae (CRE). Real-world experience with CZA in the treatment of MDR GNB is accumulating but remains limited by the small number of patients thus far described. We sought to build upon prior reports by describing the clinical characteristics and outcomes of a diverse cohort of patients with MDR GNB infections treated with CZA.

Methods. Retrospective, multicenter, cohort study of patients treated with CZA (≥72 h) for suspected or confirmed MDR GNB (resistant to ≥1 antibiotic in ≥3 classes) infections between 2015 and 2018. The primary outcome was clinical failure defined as a composite of 30-day mortality, 30-day recurrence, or worsening signs and symptoms while on CZA. Independent predictors of clinical failure were sought through multivariable logistic regression analysis.

Results. A total of 114 patients were included. The median (IQR) age was 65 (53, 74), the median Charlson Comorbidity Index was 4 (2, 6), and the median APACHE II score was 20 (14, 28). CRE and MDR *Pseudomonas aeruginosa* were isolated in 74 (66%) and 31 (28%) of cases, respectively. The predominant sources were respiratory (40%) and urinary tract (20%). Blood cultures were positive in 10% of cases. Combination therapy (≥48 h) was used in 40%. Among carbapenem-resistant *Klebsiella pneumoniae* ($n = 34$), 97% were susceptible to CZA. The resistant isolate was positive for NDM and OXA. Clinical failure, 30-day mortality, and recurrence were 28%, 13% and 5%, respectively. Independent predictors of clinical failure were immune compromise (*a*OR 6.25, 95% CI 1.30, 30.11), Glasgow Coma scale ≤ 12 (*a*OR 3.76, 95% CI 1.30, 10.88), primary bacteremia or respiratory source (*a*OR 2.96, 1.07–8.17) and age less than 65 (*a*OR 2.87, 95% CI 1.09, 7.61).

Conclusion. The use of CZA was associated with a clinical failure rate of 28% which compares favorably with historical controls of MDR GNB infections. Future investigations evaluating long-term outcomes and comparative studies are needed to more precisely define the role of CZA in MDR GNB infections.

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2380. Healthcare Resource Utilization for High-Risk Patients Treated With Dalbavancin in Physician Office Infusion Centers (POICs)

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Background. Medicare beneficiaries and patients (patients) ≥65 years comprise the highest risk for utilization of healthcare resources including emergency department (ED) visits and hospitalizations (hosp). Dalbavancin (DAL) is a long-acting lipoglycopeptide approved for treatment of bacterial skin and skin structure infections, well suited for outpatient therapy due to a 1–2 dose regimen. We investigated the use of healthcare resources following DAL with associated costs compared with national data.

Methods. A multi-center, retrospective chart review was conducted of all high-risk patients receiving DAL during 2017 at participating sites. Data included demographics, diagnosis, Charlson index, prior/post-IV therapies, DAL regimen, and adverse drug reactions (ADRs). ED visits and hosp within 30 days post-DAL were assessed and compared with Healthcare Cost and Utilization Project Nationwide Inpatient Sample and Nationwide Emergency Department Sample stratified by diagnosis. The inpatient length of stay (LOS) was used to calculate hospital charges.

Results. DAL was administered to 124 patients (mean age: 71 ± 10 years, mean Charlson index of 4.6, 55% male) in 10 POICs. Most patients (92%) received a 1-dose regimen. Diagnoses included cellulitis (32%), abscess (22%), diabetic foot infection (15%), osteomyelitis (10%), surgical site infections (9%), prosthetic device infection (9%), and musculoskeletal infections (3%). 55% were treated from the community. IV therapy with other agents was provided prior to DAL in 58% and following DAL in 6%. Moderate to severe ADRs were seen in 12 patients (10%) with 4 admitted to the ED and 3 hosp. Median onset of ADRs was 5 days post DAL. All cause ED visits were 10 (8%), compared with a national rate of 10.6% based on diagnosis and age ≥65. All cause 30-day hosp admissions were 11.3% (14/124) compared with a national rate of 16.1% based on diagnosis. Mean inpatient LOS was 4.9 days compared with 5.3 days, resulting in healthcare resource cost savings of $97,014.

Conclusion. Use of DAL in high-risk, comorbid patients treated in POICs was associated with lower usage of both healthcare resources and corresponding costs than national estimates for respective diagnoses. AEs contributed to healthcare resource use. DAL provides a convenient outpatient treatment option for high-risk patients that may save use of healthcare resources.

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2381. Ceftolozane/Tazobactam in the Treatment of Experimental *Pseudomonas aeruginosa* Pneumonia in Persistently Neutropenic Rabbits: Impact on Strains With Genetically Defined Resistance

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Background. *Pseudomonas* pneumonia is a life-threatening infection with high mortality, particularly in neutropenic patients. The efficacy of current antimicrobial therapy with extended spectrum penicillins (ESPs) and anti-pseudomonal cephalosporins (ASCs) is limited by emergence of resistance. Ceftolozane/tazobactam is a novel cephalosporin with *in vitro* activity against isolates of *Pseudomonas aeruginosa* that are resistant to ESPs and ASCs. In order to assess the antimicrobial effect of ceftolozane/tazobactam in treatment of *Pseudomonas* pneumonia, we investigated this new agent in the treatment of experimental *Pseudomonas* pneumonia in persistently neutropenic rabbits infected with different strains of genetically defined mechanisms of resistance.

Methods. *Pseudomonas* pneumonia was established in a rabbit model by direct endotracheal inoculation of *P. aeruginosa* 1×10^8–10^9 CFUs for tracheobronchial colonization that evolves into bronchopneumonia. Four treatment groups were studied: ceftolozane/tazobactam, ceftazidime (CTZ), piperacillin/tazobactam (TZP), and untreated controls (UC). Rabbits were dosed IV to achieve humanized doses of ceftolozane/tazobactam 3g (2g/1g) Q8h, CTZ 2g Q8h, and TZP 4.5g Q8h. Four isolates of *P. aeruginosa* were studied: pan-susceptible (PS), OPRD porin loss (OPRDPL), efflux pump expression (EPE), and AmpC hyperexpression (ACHE). Profound, persistent neutropenia was maintained with cytosine arabinoside and methylprednisolone. Treatment was continued for 12 days.

Results. Treatment with ceftolozane/tazobactam resulted in $\geq 10^5$ reduction in residual pulmonary bacterial burden caused by all 4 strains ($P \leq 0.01$). This antibacterial activity coincided with reduction of lung weight ($P < 0.05$), which is a marker of organism-mediated pulmonary injury. CTZ was less active in ACHE-infected rabbits, while TZP had less activity in EPE, ACHE, and OPRDPL strains. Survival was prolonged in ceftolozane/tazobactam and CTZ treatment groups in comparison to that of TZP and UC ($P < 0.001$).

Conclusion. Ceftolozane/tazobactam is highly active in treatment of experimental *P. aeruginosa* pneumonia in persistently neutropenic rabbits, including infections caused by strains with the most common resistant mechanisms.

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2382. Ceftolozane/Tazobactam for the Treatment of Multidrug-Resistant *Pseudomonas aeruginosa* Infections in Immunocompromised Patients: A Multi-Center Study

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