With Delafloxacin (DLX) vs. Vancomycin/Aztreonam (VAN/AZ)
During Treatment of Acute Bacterial Skin And Skin Structure Infection (ABSSSI)

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 were designed to receive either DLX monotherapy or VAN 15 mg/kg (actual body weight) to VAN 15 mg/kg. Patients were randomized 1:1 to receive either DLX 110 mg every 12 hours or VAN 15 mg/kg every 6 hours. Patients were then re-randomized at the end of each treatment period to either continuation of the same treatment arm or crossover to the alternate treatment arm. The primary endpoint was objective response at 48–72 hours with investigator assessment of outcomes at days 14 and 28.

Results. 850 patients were randomized in United States, Europe, Asia and Latin America. 63% were male with mean age 59 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 cm² 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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2380. Healthcare Resource Utilization for High-Risk Patients Treated With Dalbavancin in Physician Office Infusion Centers (POICs)

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Background. Healthcare providers are challenged to meet the rising incidence of antibiotic-resistant infections that are associated with an increased hospital length of stay, increased hospital charges and antimicrobial resistance. Dalbavancin (DAL), formerly known as telavancin, is a synthetic lipoglycopeptide approved for the treatment of skin and skin structure infections in adults, is indicated for patients who require hospitalization, including those requiring hospitalization due to a 1-2 dose regimen. Dalbavancin offers ease of administration and potential cost savings over traditional antibiotic therapy.

Methods. Outpatient infusion providers were interviewed for a survey on their experience of DAL with in-use infections. The survey questioned their experience with infections developed post-DAL administration, frequency of repeat infections, frequency of hospitalization during and post-DAL administration, and cost savings. The results were summarized and compared to national data.

Results. 14 providers were interviewed. Of these, 12 (86%) had experience with patients who received DAL. Of these 12, 5 (42%) had hospitalization post-DAL administration. 3 (25%) had infections post-DAL. Of these 3, 1 (33%) was due to a resistance in the organism post-DAL administration. 1 (33%) had a repeat infection post-DAL administration. Of those with repeat infections, 1 (33%) was due to a resistance in the organism post-DAL administration. Of those with hospitalization post-DAL administration, 1 (33%) resulted in an inpatient hospitalization.DAL cost savings was reported in 10 (83%) cases of outpatient infusion. DAL cost savings was reported by means of prior antibiotic comparison studies, which showed that DAL was more cost-effective than similar antibiotics. DAL cost savings was also reported by means of hospitalization rates, as patients were able to avoid hospitalization post-DAL administration.

Conclusion. DAL, when administered by experienced outpatient infusion providers, may provide cost savings and decreased hospitalization rates for the treatment of skin and skin structure infections in adults. Outpatient infusion providers can provide a valuable treatment option for patients with skin and skin structure infections.

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. P. aeruginosa pneumonia is a life-threatening infection with high mortality, particularly in neutropenic patients. The efficacy of current antimicrobial therapies in patients with extended spectrum β-lactamases (ESβ) and anti-pseudomonal β-lactams against different strains of P. aeruginosa (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 ESβs and ASCs. In order to assess the antimicrobial effect of ceftolozane/tazobactam in treatment of P. aeruginosa pneumonia, we investigated this new agent in the treatment of experimental P. aeruginosa pneumonia in persistently neutropenic rabbits infected with different strains of genetically defined mechanisms of resistance.

Methods. P. aeruginosa pneumonia was established in a rabbit model by direct endotracheal inoculation of P. aeruginosa 1 x 10^8-10^10 CFUs for tracheobronchial colonization that evolves into bronchopneumonia. Four treatment groups were studied: ceftolozane/tazobactam, ceftaridine (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), OPN3 porin loss (OPRDP1), eflux pump expression (EPE), and AmpC hyperexpression (ACHE). Pseudomonas aeruginosa was maintained with cystine arabinose and methy1prednisolone. Treatment was continued for 12 days.

Results. Treatment with ceftolozane/tazobactam resulted in ≥10^3 reduction in residual pulmonary bacterial burden caused by all 4 strains (P ≤ 0.01). This antibacterial activity coincided with reduction of lung weight (P < 0.05), which is a marker of organ-related pulmonary toxicity. CTZ was less active in ACHE-infected rabbits, while TZP had less activity in EPE, ACHE, and OPDP1 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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Background. P. aeruginosa Infections In Immunocompromised Patients: A Multi-Center Study

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