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**Session:** 51. Soft Tissue and Skin Infections  
**Thursday, October 3, 2019: 12:15 PM**

**Background.** Recently, overall reductions for invasive MRSA infections (isolation from a normally sterile site) have slowed. Healthcare-associated community-onset (HACO) invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infections are those with recent healthcare exposures who develop MRSA infection outside acute care hospitals, and account for most invasive MRSA infections. HACO incidence decreased 6.6% per year during 2005–2008; the contribution of persons who inject drugs (PWID) to HACO incidence has not been reported.

**Methods.** We identified invasive MRSA infections using active, population- and laboratory-based surveillance data during 2009–2017 from 25 counties in 7 sites (CA, CT, GA, MD, MN, NY, TN). Cases were HACO if culture was obtained from an outpatient, or  $\leq 3$  days after hospitalization in a patient with  $\geq 1$  of the following healthcare exposures (HEs): hospitalization, surgery, dialysis, or residence in a long-term care facility (LTCF) in the past year; or central vascular catheter  $\leq 2$  days before culture. We calculated incidence (per census population) overall, for PWID cases and others, and for cases associated with each HE. For each HE, we calculated the proportion of overall incidence increase for PWID and others.

**Results.** HACO MRSA incidence declined overall from 2009 to 2016 but increased from 2016 to 2017 overall (8%), for both PWID (63%) and others (5%) (figure). For both PWID and non-PWID, incidence from 2016 to 2017 increased by 0.5 cases/100,000 population; 91% of the increase in PWID occurred in cases with a past year hospitalization while 78% of the increase in cases not associated with injection drug use (IDU) occurred in cases with past year LTCF residence. Past year LTCF residence was less common among PWID (16%) than among other cases (38%,  $P < 0.01$ ).

**Conclusion.** After years of declines, HACO MRSA incidence increased equally in 2017 for cases associated with IDU and in cases unrelated to IDU. Increases in PWID-associated cases account for half the overall increase, indicating that efforts to reduce HACO MRSA should address PWID risk factors as these infections may be due to self-injection. In addition, increases not related to PWID, if sustained, would be a reversal of historic trends and require further investigation into causes.

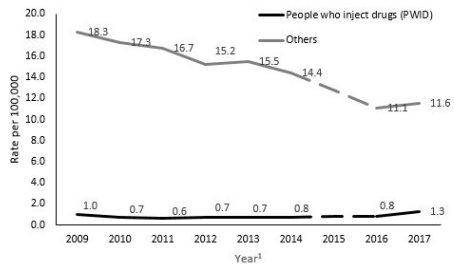


Figure. Invasive healthcare-associated community-onset methicillin-resistant *Staphylococcus aureus* rate per census population by year, for cases associated with people who inject drugs (PWID), and cases not associated with PWID, 2009–2017.

<sup>1</sup>Not all sites reported data in 2015.

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#### 470. Treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI) in Patients with Significant Drug Abuse: Outcomes from Global Phase 3 Studies of Delafloxacin (DLX)

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**Background.** Delafloxacin (DLX), an IV/oral anionic fluoroquinolone antibiotic, is approved for the treatment of ABSSSI including those due to MRSA and Gram-negative pathogens including *P. aeruginosa*. Two global phase 3 ABSSSI trials included patients with substance abuse including IV drugs.

**Methods.** Two multicenter, double-blind, double-dummy trials of adults with ABSSSI randomized patients 1:1 to receive either DLX monotherapy or vancomycin 15 mg/kg + aztreonam (VANAZ) 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  $\geq 20\%$  reduction in lesion size, and Investigator assessment of outcome at Follow-up (FU, Day 14), both in the Intent To Treat population.

**Results.** In the 2 studies, 620 patients with substance abuse, excluding alcoholism, including heroin, cocaine and methamphetamine abuse, were randomized in the United States. 71% were male with mean age 44 years. Average erythema area at baseline was  $\sim 230$  cm<sup>2</sup>. 16% percent had cellulitis, 30% abscesses, and 53% wound. *S. aureus* (SA) was the most frequent pathogen. DLX was non-inferior to VANAZ for the Objective Response: 85.9% DLX vs. 84.4% VANAZ [ $\Delta 2.6$  (95% CI -2.9, 8.1)] as well as the assessment of outcome at FU: 82.0% DLX vs. 79.3% VANAZ [ $\Delta 3.2$  95% (CI -3, 9.4)]. Micro

success in evaluable patients with SA was seen in 99.1% DLX vs. 100% VANAZ as well as 98.2% DLX vs. 100% VANAZ in patients with MRSA. The overall % of patients with at least one adverse event (AE) was comparable for DLX (49.0%) compared with VANAZ (56.1%). The most frequent treatment-related AEs were gastrointestinal in nature, including nausea seen in 9.7% DLX and 5.8% VANAZ patients, primarily mild to moderate in severity. There were no cases of *C.difficile* diarrhea. Discontinuations due to treatment-related AEs were lower with DLX (0.3%) compared with VANAZ (2.2%).

**Conclusion.** Fixed-dose monotherapy DLX was comparable to VANAZ in treatment of ABSSSI in patients with substance abuse based on the Objective Response as well as investigator-assessed outcome. DLX was also comparable to VANAZ in treating patients with SA and MRSA. DLX appears effective and well tolerated in patients with ABSSSI and significant substance abuse.

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

#### 471. Safety and Efficacy of Oral and/or Intravenous Tedizolid Phosphate (TZD) in Adolescents with Acute Bacterial Skin and Skin Structure Tissue Infections (ABSSSI)

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**Background.** Tedizolid phosphate has activity against gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus*, and was approved for the treatment of ABSSSI in adults in 2014. This study compared the safety and efficacy of TZD with protocol-specified, active comparators for the treatment of ABSSSI in adolescents.

**Methods.** This was a randomized, assessor-blind, global, multicenter, phase 3 study of TZD vs. active comparator for the treatment of gram-positive ABSSSI in adolescents (aged 12 to < 18 years; NCT02276482). Enrolled patients were stratified by region and randomized 3:1 to TZD 200 mg (IV and/or oral) once daily for 6 days or investigator-selected active comparator per local standard of care (IV vancomycin, linezolid, clindamycin, flucloxacillin, or cefazolin, and/or oral linezolid, clindamycin, flucloxacillin, or cephalixin) for 10 days. The primary endpoint was safety. The percentages of patients with treatment-emergent adverse events (TEAEs) were documented; secondary efficacy endpoints included the blinded investigator’s assessment of clinical success at a test of cure visit (18–25 days after start of dosing) and early clinical response ( $\geq 20\%$  reduction from baseline lesion area) at 48–72 h. No hypothesis testing was planned for the treatment groups.

**Results.** Of the 121 patients enrolled, 120 were treated (TZD,  $N = 91$ ; comparator,  $N = 29$ ). Median (range) age was 15 (12–17) years. Most patients were male (62.5%), white (86.7%), and enrolled in Europe (78.3%). Infections included major cutaneous abscess (42.5%), cellulitis/erysipelas (40.0%), and infected wound (17.5%). At baseline, the median (range) lesion surface area was 82.1 (14–978) cm<sup>2</sup>. Of those with gram-positive cultures ( $n = 64$ ), *S. aureus* was most frequently isolated ( $n = 55$  [85.9%]) with 3 isolates (4.7%) being methicillin resistant. TZD was well tolerated, and TEAEs were balanced between treatment arms (TZD, 14.3%; comparator, 10.3%). A total of 3 (3.3%) patients in the TZD group and 1 (3.4%) in the comparator group experienced a single-drug-related TEAE. Clinical success rates were high and similar between treatment groups (table).

**Conclusion.** TZD demonstrated comparable safety and efficacy to comparator in the treatment of ABSSSI in adolescents.

Table. Efficacy Outcomes

Outcome	Analysis Set	Response	TZD	Comparator	Difference, % (95% CI) <sup>a</sup>
Investigator-assessed clinical response at TOC	ITT, N		91	29	
		Clinical success, <sup>b</sup> n (%)	88 (96.7)	27 (93.1)	3.6 (-6.3, 13.5)
		95% CI <sup>c</sup>	(90.7, 99.3)	(77.2, 99.2)	
Programmatic early clinical response at 48–72 h	CE, N		87	27	
		Clinical success, <sup>b</sup> n (%)	87 (100)	26 (96.3)	3.7 (-3.4, 10.8)
		95% CI <sup>c</sup>	(95.8, 100)	(81.0, 99.9)	
Programmatic early clinical response at 48–72 h	ITT, N		91	29	
		Success/responder, <sup>d</sup> n (%)	84 (92.3)	28 (96.6)	-4.2 (-12.9, 4.4)
		95% CI <sup>c</sup>	(84.8, 96.9)	(82.2, 99.9)	

CE, clinically evaluable; CI, confidence interval; ITT, intent-to-treat; TOC, test of cure; TZD, tedizolid phosphate.

<sup>a</sup>The difference (TZD minus comparator) in the clinical success rate and 95% CI calculated using the unstratified method of Miettinen and Numminen.

<sup>b</sup>Met all of following criteria: Resolution or near resolution of most disease-specific signs and symptoms; absence or near resolution of regional or systemic signs of infection (lymphadenopathy, fever,  $>10\%$  immature neutrophils, abnormal white blood cell count), if present at baseline; no new signs, symptoms, or complications attributable to the infection under study (no further antibiotic therapy required for the treatment of the primary lesion).

<sup>c</sup>An exact 2-sided 95% CI determined for the rate of clinical success in each treatment group using the Clopper-Pearson method.

<sup>d</sup>Minimum  $\geq 20\%$  reduction from baseline lesion area.

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