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Delafloxacin (DLX) is effective and well-tolerated in treatment of obese patients with acute bacterial skin and skin structure infections (ABSSSI) versus vancomycin/aztreonam (VAN/AZ)

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Background: DLX, an investigational anionic fluoroquinolone antibiotic with activity against Gram-positive and Gram-negative pathogens, including MRSA, is in development for treatment of ABSSSI. Two global phase 3 ABSSSI trials (studies 302 and 303) included obese patients (BMI≥ 30kg/m^2).

Material/methods: Two multicenter, double-blind, double-dummy trials of adults with ABSSSI randomized patients 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 300mg BID IV only; study 303 used DLX 300mg BID IV for 3 days with a mandatory blinded switch to DLX 450mg 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 2 studies, 639 obese patients were randomized in US, Europe, Latin America and Asia. 56% were male with mean age 51 yrs. Average erythema area at baseline was 408 cm^2. 55

percent had cellulitis, 22% abscesses, 23% wound and 1% burn infections. 53% of patients had *S. aureus* with over a third being MRSA. Patients were treated for a median of 6 days. Key endpoints are shown below:

Key Endpoints	DLX	VAN/AZ	DLX – VAN/AZ (95% CI) stratified by study
	n/Total (%)	n/Total (%)	
Objective response 48-72h (ITT)	266/331 (80.4%)	244/308 (79.2%)	1.7 (-4.5, 7.9)
Investigator-Assessed Success (FU ITT)	285/331 (86.1%)	262/308 (85.1%)	1.3 (-4.2, 6.8)
Investigator-Assessed Success (LFU ITT)	278/331 (84.0%)	250/308 (81.2%)	3.1 (-2.9, 9.0)
Micro Success (FU ME) for *S aureus*	99/101 (98.0%)	64/69 (92.8%)	8.4 (0.6, 16.2)
Micro Success (FU ME) for MRSA	40/40 (100%)	19/21 (90.5%)	15.4 (-1.2, 32.0)

The overall % of patients with at least one treatment-emergent AE (TEAE) was comparable for DLX (44.3%) compared to VAN/AZ (42.8%). The most frequent treatment-related adverse events were gastrointestinal in nature including diarrhea seen in 6.1% of DLX and nausea seen in 4.6% of VAN/AZ patients, which were primarily mild to moderate in severity. There was one case of *C.difficile* diarrhea. Discontinuations due to treatment related AEs were lower with DLX (0.6%) compared to VAN/AZ (2%).

Conclusions: Fixed dose monotherapy DLX was comparable to VAN/AZ combination therapy in treatment of ABSSSI in obese patients based on the early objective response as well as investigator-assessed response at FU and LFU. DLX was also comparable to VAN/AZ in treating patients with *S. aureus*. DLX appears effective and well tolerated in obese patients with ABSSSI.