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Delafloxacin (DLX) is effective and well-tolerated in treatment of diabetic (DM) 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 included DM patients (studies 302 and 303).

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 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 2 studies, 164 DM patients were randomized in US, Europe, Latin America and Asia. 59% were male with mean age 59 yrs. Average erythema area at baseline was 424 cm^2. 60% had cellulitis, 24% abscesses, 15% wound and 1% burn infections. 52% of patients had *S. Aureus*, and

over a third were MRSA. ~12% of patients had baseline Gram-negative pathogens. 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)	63/83 (75.9%)	63/81 (77.8%)	-1.4 (-14.4, 11.6)
Investigator-Assessed Success (FU ITT)	71/83 (85.5%)	68/81 (84.0%)	2.2 (-9.2, 13.6)
Investigator-Assessed Success (LFU ITT)	71/83 (85.5%)	69/81 (85.2%)	1.7 (-9.5, 12.9)
Micro Success (FU ME) for *S aureus*	20/23 (87.0%)	22/25 (88.0%)	-1.6 (-23.4, 20.3)

The overall % of DM patients with at least one treatment-emergent AE (TEAE) was lower for DLX (41.7%) compared to VAN/AZ (50.6%). The most frequent treatment-related adverse events were gastrointestinal in nature including diarrhea seen in 7.1% and 4.8% of DLX and VAN/AZ patients respectively and was generally mild to moderate in nature. There were no cases of *C.difficile* diarrhea. There were no reports of treatment-related dysglycemias. There were no discontinuations on DLX due to AEs, but 6% of VAN/AZ-treated DM patients discontinued due to AEs.

Conclusions: In DM patients, fixed dose DLX monotherapy was comparable to VAN/AZ combination therapy in treatment of ABSSSI 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 DM patients with ABSSSI.