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Oral Session
New antibiotics in clinical trials

COMPARISON OF THE MICROBIOLOGICAL EFFICACY OF TEDIZOLID AND LINEZOLID IN THE ESTABLISH-1 AND ESTABLISH-2 PHASE 3 CLINICAL TRIALS

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Objective: To compare microbiological response with tedizolid, a novel oxazolidinone, versus linezolid against common causative pathogens in acute bacterial skin and skin structure infections (ABSSSIs) using pooled data from the ESTABLISH-1 and ESTABLISH-2 clinical trials.

Methods: ESTABLISH-1 and ESTABLISH-2 were randomised, double-blind, phase 3 clinical trials evaluating efficacy and tolerability of tedizolid phosphate (200 mg once daily for 6 days; N=664 patients) versus linezolid (600 mg twice daily for 10 days; N=669 patients) in the treatment of patients with ABSSSIs (total intent-to-treat [ITT] population, 1,333 patients). Microbiological samples were obtained from ABSSSI sites and blood samples at baseline and at end-of-treatment (EOT; day 11 relative to the first dose of study drug on day 1) and the post-therapy evaluation (PTE; 7-14 days after EOT). The pooled microbiological ITT (micro-ITT) population included all patients from both studies who had Gram-positive bacteria know n to cause ABSSSI (tedizolid, n=406; linezolid, n=412). Favourable microbiological outcomes at EOT and PTE visits were defined as eradication (i.e. absence of original baseline pathogens) or presumed eradication (i.e. no source specimen to culture in a patient assessed as a clinical success, based on the programmatic determination of clinical response at EOT or on the investigator assessment of clinical response at PTE).

Results: Baseline Gram-positive aerobic organisms w ere identified in 399/406 (98.3%) tedizolid and 405/412 (98.3%) linezolid patients, including *Staphylococcus aureus* (81.0% and 83.0%, respectively) and *Streptococcus pyogenes* (8.1% and 4.9%, respectively). Methicillin-resistant *S aureus* (MRSA) and methicillin-sensitive *S aureus* (MSSA) accounted for 34.7% and 46.3% of infections, respectively, in the tedizolid arm and for 35.4% and 48.1% of infections, respectively, in the linezolid arm. The minimum inhibitory concentration for tedizolid ranged from 0.12 mg/L to 0.5 mg/L for *Staphylococcus* spp and ≤0.015 mg/L to 0.25 mg/L for *Streptococcus* spp; the corresponding values for linezolid were 1 mg/L to 4 mg/L and ≤0.06 mg/L to 1 mg/L, respectively. The minimum inhibitory concentration against 90% (MIC_{90}) of *S aureus* isolates w as 0.25 mg/L for tedizolid and 2 mg/L for linezolid; the corresponding MIC_{90} values against *S pyogenes* were 0.25 mg/L for tedizolid and 1 mg/L for linezolid. In the micro-ITT population, the overall favourable microbiological response rate in both treatment arms was approximately 90% at EOT and approximately 87% at PTE. The microbiological response for key target pathogens at EOT and PTE (per baseline pathogen) is summarised in the Table.

T)	gical Response per Pathogen (micro-I
Linezolid n/N1 (%)	Tedizolid n/N1 (%)
nse at EOT visit	
310/342 (90.6)	299/329 (90.9)
124/146 (84.9)	121/141 (85.8)
188/198 (94.9)	178/188 (94.7)
19/20 (95.0)	32/33 (97.0)
nse at PTE visit	
304/342 (88.9)	292/329 (88.8)
120/146 (82.2)	119/141 (84.4)
186/198 (93.9)	173/188 (92.0)
19/20 (95.0)	30/33 (90.9)
e.	ients with specified pathogen at baselir

Conclusion: Based on the observed minimum inhibitory concentrations, tedizolid was four-to eight-fold more active than linezolid against *Staphylococcus* spp, including MRSA, and *Streptococcus* spp. Overall, high rates of favourable microbiological responses were observed in the tedizolid and linezolid treatment arms at the EOT and PTE visits.