**O192**

**2-hour Oral Session**

**New antibacterial agents - phase 2 and phase 3 clinical trials**

## Efficacy and safety of tedizolid versus linezolid in patients with complicated skin and soft tissue infection after IV, IV/oral, or oral administration

C. De Anda[1], T. Sandison[1], S. Anuskiewicz[1], P. Prokocimer[1]

[1]*Cubist Pharmaceuticals, San Diego, USA*

**Objectives**: Two Phase 3 trials, ESTABLISH-1 and ESTABLISH-2, demonstrated the noninferior efficacy of tedizolid (200 mg once daily for 6 days) to linezolid (600 mg twice daily for 10 days) in patients with complicated skin and soft tissue infections (cSSTI). Because of high bioavailability, IV and oral formulations of tedizolid can be used interchangeably without dose adjustments. We evaluated the efficacy and safety of tedizolid versus linezolid in patients receiving IV administration only, initial IV followed by oral administration, or oral-only administration using pooled data from both trials.

**Methods:** ESTABLISH-1 patients received oral therapy only, whereas ESTABLISH-2 patients received IV therapy with an option to switch to oral therapy after 24 hours. Key efficacy measures were early clinical response (≥20% reduction from baseline in lesion area at 48-72 hours after start of therapy) and investigator-assessed clinical response at post-therapy evaluation (PTE; 7 to 14 days after end of therapy). Safety assessments included incidence of treatment-emergent adverse events (TEAE).

**Results:** Baseline disease severity as measured by mean lesion surface area was similar between tedizolid and linezolid patients in the IV-only, IV/oral, and oral-only subgroups. Rates of methicillin-resistant *Staphylococcus aureus* (MRSA) infection were higher in the oral-only group (IV only, 4.9%; IV/oral, 18.9%; oral only, 26.7%) due to the higher prevalence of MRSA in ESTABLISH-1, which had ~80% US enrollment. In ESTABLISH-2, no differences were noted between tedizolid and linezolid groups in mean time to oral switch (1.7 vs 1.8 days) or proportion of patients receiving ≥2 days of IV therapy (72% vs 69%) or IV therapy for the duration of treatment (19% vs 17%). Rates of early clinical response and investigator-assessed response at PTE were similar among the 3 treatment subgroups for tedizolid and linezolid (**Table**). Infusion-site reactions were rare in both treatment groups (tedizolid, 1.5%, linezolid, 2.1%).

**Conclusion:** Early and late clinical response rates were high in cSSTI patients treated with tedizolid, regardless of administration route. These findings underscore the usefulness of tedizolid for sequential or all-oral therapy, potentially allowing for shorter hospitalization, fewer hospitalization-related complications, and cost savings.

| Route of Administration | Tedizolid n/N (%) | Linezolid n/N (%) | Difference (95% CI) |
|---|---|---|---|
| **Early clinical response** | | | |
| IV only | 54/64 (84.4) | 48/58 (82.8) | 1.6 (–11.6, 14.8) |
| IV/oral | 229/268 (85.4) | 228/276 (82.6) | 2.8 (–3.3, 9.0) |
| Oral only | 259/332 (78.0) | 255/335 (76.1) | 1.9 (–4.5, 8.3) |
| **Clinical response at PTE** | | | |
| IV only | 53/64 (82.8) | 49/58 (84.5) | –1.7 (–14.8, 11.5) |
| IV/oral | 239/268 (89.2) | 244/276 (88.4) | 0.8 (–4.5, 6.1) |
| Oral only | 284/332 (85.5) | 288/335 (86.0) | –0.4 (–5.7, 4.9) |

PTE, post-therapy evaluation.