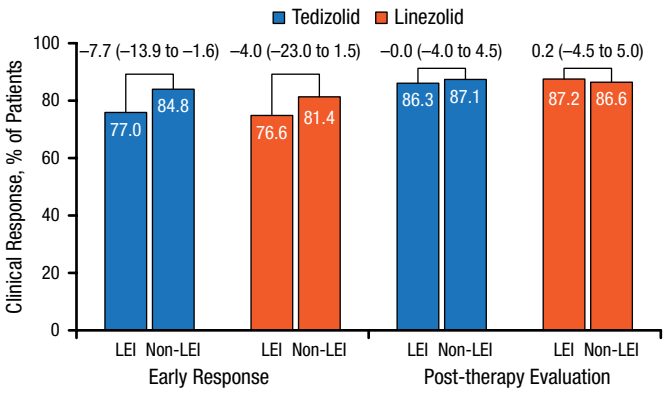
Figure 5. Early and Post-therapy Response Rates in Patients With Lower- and Non–Lower-Extremity Locations



Values above brackets indicate treatment difference (95% CI).

LEI, lower-extremity infection.

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Table 1. Clinical Responses in Patients With and Without Baseline Pathogen Isolation Treated With Tedizolid

	No Pathogen Isolated at Baseline			
	Microbiology Attempted, but No Result (n = 207)	Microbiology Not Attempted (n = 51)	Overall (n = 258)	Pathogen Isolated at Baseline[a] (n = 406)
Early clinical response	165 (79.7)	37 (72.5)	202 (78.3)	340 (83.7)
Investigator-assessed response at EOT	185 (89.4)	49 (96.1)	234 (90.7)	365 (89.9)
Investigator-assessed response at PTE	178 (86.0)	48 (94.1)	226 (87.6)	350 (86.2)

Data presented in n (%).

EOT, end of therapy; PTE, post-therapy evaluation.

[a]MicroITT population (all patients with at least 1 gram-positive pathogen isolated at baseline).

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baseline with that in patients who did have a confirmed pathogen. Using the same pooled data, tedizolid appeared to be an effective option for the treatment of ABSSSIs regardless of whether a causative pathogen was identified at baseline.

Of the 664 patients randomized to tedizolid, 258 did not have a pathogen isolated at baseline. Microbiologic assessments were attempted in 207 patients with inconclusive results; in 51 patients, microbiologic assessments were not attempted. This latter group of patients had substantially larger lesion areas. Most infections were located in the lower extremities (54.7%) and diagnosed as cellulitis/erysipelas (76%).

Tedizolid remains an effective treatment regardless of whether a pathogen had been isolated at baseline (Table 1).

There were no differences in AEs, TEAEs, drug-related TEAEs, serious TEAEs, or TEAEs leading to discontinuation between tedizolid-treated patients regardless of the identification of a baseline pathogen. The most frequent TEAEs in patients with unknown pathogens were nausea (8.5%), headache (5.8%), and diarrhea (4.3%). Nausea (7.9%), abscess (7.7%), and headache (6.4%) were the most common TEAEs in patients with known baseline pathogens.

Tedizolid was generally well tolerated in patients with ABSSSIs regardless of whether a causative pathogen was identified, the route of administration, or the location of the infection. Only rarely was treatment discontinued due to AEs. Overall, the most common TEAEs were nausea, headache, diarrhea, vomiting, and abscess. Tedizolid has a high bioavailability and, with its route of administration variability, may allow for shorter hospitalizations, fewer hospitalization-related complications, and cost savings.

Additional Results From SECURE: Comparing Isavuconazole With Voriconazole

Written by Jill Shuman

Isavuconazole (ISA) is a novel, water-soluble, broad-spectrum triazole antifungal agent developed for the treatment of invasive fungal diseases (IFDs), including invasive aspergillosis. These are rare infections that occur typically in immunocompromised, critically ill patients. By disrupting fungal membrane structure and function, ISA is active against all major opportunistic and pathologic fungi [Seyedmousavi S et al. *Expert Rev Anti Infec Ther*. 2015]. ISA was approved by the FDA for the treatment of aspergillosis and mucormycosis in March 2015.

The SECURE trial [NCT00412893] investigated the safety and efficacy of ISA as compared with voriconazole (VRC) in patients with IFD caused by *Aspergillus* spp and other filamentous fungi. SECURE was a large (n = 516) phase 3 double-blind randomized trial that demonstrated the noninferiority of ISA compared with VRC for all-cause mortality at day 42 in the intention-to-treat population (ISA, 18.6%; VRC, 20.2%; 95% CI, –7.8 to 5.7) [Maertens J et al. ECCMID 2014 (abstr O230a)].

Two presenters in this session reported additional, more detailed safety and outcomes data from SECURE. Andrew J. Ullmann, MD, University of Würzburg, Würzburg, Germany, presented information regarding the development of treatment-emergent adverse events (TEAEs) in both the ISA and VRC groups. A TEAE was defined as any adverse event after the first administration of the drug until 28 days following the last administration.

Among patients in the ISA group, 96% experienced at least 1 TEAE, compared with 98% in the VRC group. This was an expected finding related to the severity of the patients' underlying illnesses. However, when analyzed by system organ class, moderate or severe TEAEs in the ISA group were lower in 19 of the 24 classes. In the comparison of the ISA and VRC groups, a significant difference was seen in disorders of the eye (15% vs 27%; $P < .01$), skin (33% vs 42%; $P < .05$), and hepatobiliary system (9% vs 16%; $P < .05$). Overall, the rate of treatment-related TEAEs was significantly lower in the ISA group than the VRC group (42% vs 60%, $P < .01$). Psychiatric (27% vs 33%) and cardiac (17% vs 22%) events were also lower in the ISA group vs the VRC group; however, this difference was not statistically significant.

Prof Ullmann suggested that the difference in TEAEs favoring ISA was influenced primarily by 4 factors: disorders of the eye, the hepatobiliary system, investigations (including elevations in hepatic enzymes), and psychiatric disorders.

Debra Goff, PharmD, Ohio State University, Columbus, Ohio, USA, presented safety and outcomes in obese patients (body mass index [BMI] ≥ 30 kg/m^2) enrolled in the SECURE trial. The analysis was done on patients with proven/probable IFD treated with either ISA or VRC who were categorized into 3 BMI classifications: < 25, 25 to < 30, and ≥ 30 kg/m^2.

Of the 527 randomized patients, 263 had proven/probable IFD and BMI data available; 25 patients were obese (ISA, n = 15; VRC, n = 10). All-cause mortality through day 42 was comparable between treatment arms in obese patients (1 vs 2 patients; adjusted difference, –13.3; 95% CI, –50.9 to 24.2). Similar numbers of obese patients responded successfully to either ISA or VRC (6 vs 4; adjusted difference, 0.0; 95% CI, –49.4 to 49.4). Drug-related TEAEs (40% vs 70%), serious TEAEs (53% vs 90%), and deaths (27% vs 40%) were less frequent in obese patients treated with ISA compared with VRC.

Dr Goff concluded that in this small subgroup of obese patients, ISA outcomes were comparable with VRC and similar to those of the other BMI subgroups. Among a small group of obese patients, there were fewer drug-related TEAEs, serious TEAEs, and deaths reported in those treated with ISA vs VRC.

Isavuconazole Safe, Effective in Treatment of IA in Patients With Renal Insufficiency

Written by Brian Hoyle

Two analyses of the pooled data from the global phase 3 multicenter VITAL [NCT00412893] and SECURE [NCT00634049] trials have demonstrated the safety and effectiveness of the broad-spectrum triazole antifungal drug isavuconazole (ISA) in the treatment of invasive aspergillosis (IA) in patients with renal impairment. Renal dysfunction can occur in up to 40% of those with IA. ISA, which is available orally as water-soluble isavuconazonium sulfate, overcomes the limitations of other intravenous drugs available to treat IA that are associated with increased risk of renal toxicity in patients with preexisting renal dysfunction [Baddley J et al. *Clin Infect Dis*. 2010; Vandewoude K et al. *J Hosp Infect*. 2004].

SECURE was a double-blind, parallel-group noninferiority trial that compared ISA and voriconazole in the treatment of IA and, more broadly, invasive fungal disease in 527 patients. Some of these patients had renal impairment. VITAL was an open-label trial involving 149 patients, and it examined the use of ISA in both fungal diseases. Both trials used a loading dose of ISA (200 mg TID intravenously on days 1 and 2), followed by ISA 200 mg QD intravenously or orally from day 3 to the end of treatment (days 84 and 180 in SECURE and VITAL, respectively). Patients were aged ≥ 18 years with proven/probable IA, with or without renal impairment at baseline. The key end point was all-cause mortality through day 42. Secondary end points included all-cause mortality and probability of survival through day 84. Treatment success was the partial or complete resolution of clinical symptoms, physical findings, and radiological abnormalities. The type, frequency, and severity of treatment-emergent adverse effects (TEAEs) were recorded.

One of the pooled analyses was presented by Johan Maertens, MD, PhD, UZ Leuven, Leuven, Belgium. This analysis focused on 143 patients of the 676 in the pooled population who had proven/probable IA treated with ISA. Thirty-one patients had renal impairment, and the remaining 112 did not. Patient characteristics at baseline are summarized in Table 1.

All-cause mortality was similar in patients with (n = 31) or without (n = 112) renal impairment at baseline through day 42 (4 [13%] vs 21 [19%]) and day 84 (8 [26%] vs 32 [29%], respectively). Overall successful response to treatment was similar in patients with (10 [32%]) and without (40 [36%]) renal impairment. The probability of survival determined by the Kaplan-Meier method