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Complicated Skin and Skin Structure Infections: Preliminary Results from the Telavancin Observational Use Registry (TOUR™)

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INTRODUCTION AND PURPOSE

- Complicated skin and skin structure infections (cSSSI) are becoming increasingly difficult to treat due to resistant Gram-positive organisms, and it is important to characterize effective treatment options for these infections[1]
- Telavancin (TLV) is a lipoglycopeptide antibacterial active against susceptible Gram-positive pathogens, including methicillin-sensitive and -resistant *Staphylococcus aureus* (MSSA and MRSA), that is administered intravenously once daily, and is suitable for both inpatient and outpatient use[2-4]
- In the US, TLV is approved in adults for the treatment of cSSSI and hospital-acquired bacterial and ventilator-associated bacterial pneumonia (HABP/VABP) when alternative treatments are not suitable[4]
- In Canada and Russia, TLV is approved for cSSSI and HABP/VABP, while in the European Union, TLV is approved for the treatment of nosocomial pneumonia, known or believed to be caused by MRSA when other alternative medicines are unsuitable[5,6]
- Telavancin provided comparable efficacy to vancomycin in a limited number of patients with either cSSSI or HABP/VABP and concurrent *Staphylococcus aureus* bacteremia[4]
- The Telavancin Observational Use Registry (TOUR™) is a multicenter registry designed to characterize real-world TLV usage patterns to assess population characteristics and clinical outcomes associated with its use for Gram-positive infections[7]
- Here we present the characteristics, TLV dosing patterns, and clinical outcomes for a subset of TOUR™ patients with cSSSIs

METHODS

TOUR™ Design and Methodology

- TOUR™ collected data from approximately 1155 patients from 46 US hospitals or outpatient infusion centers
- Any patient who received at least 1 dose of TLV after January 1, 2015, was eligible for inclusion (individuals who participated in any TLV clinical study were excluded)
- All treatment decisions and clinical assessments were at the discretion of the treating physician, and data were obtained via retrospective medical chart review

Data Collection and Analyses

- Data including demographics, primary infection type, baseline pathogens, duration of hospitalization, prior or concomitant antimicrobial treatment, TLV dosing regimen, clinical response, adverse events (AEs) of interest, and 28-day mortality were entered directly into electronic case report forms
- Adverse event data collection was limited to renal AEs and AEs leading to discontinuation or a fatal outcome
- Clinical outcome at end of therapy was designated as positive clinical response (cured or improved to step-down therapy), nonevaluable (indeterminate, missing, or undocumented), or failure
- Descriptive analyses were performed

RESULTS

- At the preliminary cutoff date of September 30, 2016, data had been collected from 36 sites for 593 patients, 279 (47%) of them with cSSSIs (**Table 1**)
- The cSSSI subtypes are listed in **Table 2**
- Common comorbidities were hypertension (129 [46.2%]) and type 2 diabetes mellitus (84 [30.1%])
- The predominant baseline pathogen was MRSA (**Table 3**)
- The median TLV dose and duration of treatment were 8.7 mg/kg (interquartile range [IQR] 7.1, 10.0) and 10.0 days (IQR 5, 17 days), respectively (**Table 4**)
- Patients were dosed as per their baseline creatinine clearance levels (**Table 5**)
- Telavancin was used as a salvage therapy in 173 (62.0%) patients
- The majority of patients (170 [60.9%]) were treated as outpatients (**Table 6**)
- Positive clinical response at the end of TLV therapy was observed in 75.3% of patients, while 9.3% of patients failed treatment and 15.4% were nonevaluable (**Figure 1**)
- Of the 279 patients (amendment 1–46, amendment 2–233), a total of 29 patients had at least 1 AE of interest (**Table 7**), 3 had 1 or more serious AEs, 20 had an AE that led to drug discontinuation, and no deaths were reported

Table 1. Baseline Demographics and Clinical Characteristics

Characteristic	Frequency (N = 279)
Age (years)*	
Mean (SD)	55.6 (14.15)
Median (range)	56 (18–88)
Age distribution, n (%)	
<65 years	193 (71.7)
≥65 years	76 (28.3)
Sex, n (%)	
Male	126 (45.2)
Female	153 (54.8)
Ethnicity, n (%)	
Hispanic or Latino	6 (2.2)
Not Hispanic or Latino	266 (95.3)
Not Reported or Unknown	7 (2.5)
Race, n (%)	
American Indian or Alaskan Native	2 (0.7)
Asian	1 (0.4)
Black or African American	30 (10.8)
White	241 (86.4)
Other	5 (1.8)
Height (cm)†	
Mean (SD)	170.5 (11.16)
Median (range)	170.2 (137.2–198.1)
Weight (kg)†	
Mean (SD)	94.5 (32.35)
Median (range)	89.8 (34.5–341.9)
BMI (kg/m²)‡	
Mean (SD)	32.6 (11.05)
Median (range)	30.7 (14.9–105.2)

Measurements not recorded for *10, †4, and ‡5 patients
BMI, body mass index; SD, standard deviation

Table 2. Complicated Skin and Skin Structure Infections

Infection Type	Frequency (%)
Cellulitis	141 (50.5)
Abscess	62 (22.2)
Surgical wound	43 (15.4)
Ulcer	16 (5.7)
Burn	6 (2.2)
Trauma	8 (2.9)
Other*	3 (1.1)
Total	279 (100)

*Other complicated skin and skin structure infections cases included 1 case of pyomyositis and 2 cases of Bursitis

Table 3. Gram-positive Baseline Pathogens

Pathogen*	Frequency (%)
Methicillin-resistant *Staphylococcus aureus*	84 (30.1)
Methicillin-sensitive *Staphylococcus aureus*	26 (9.3)
Coagulase-negative Staphylococcus	18 (6.5)
Enterococcus faecalis	5 (1.8)
Group A Streptococcus	4 (1.4)
Streptococcus anginosus Group	4 (1.4)
Enterococcus faecium	2 (0.7)
Group B Streptococcus	1 (0.4)

*67 patients reported other pathogens. More than 1 pathogen was detected in 194 patients, with Gram-negative pathogens, including Acinetobacter spp., *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* isolated as a part of a mixed Gram-positive and Gram-negative infection. Baseline pathogen was not recorded in 85 patients

Table 4. Telavancin Dosing and Treatment Duration

Telavancin Exposure Characteristics	Patients (N = 279)
Average daily dose (mg)*	
Mean (SD)	772.7 (227.83)
Median (IQR)	750.0 (750.0, 750.0)
Average daily dose per body weight (mg/kg)†	
Mean (SD)	8.5 (2.06)
Median (IQR)	8.7 (7.1, 10.0)
Duration of TLV dosing (days)*	
Mean (SD)	14.2 (16.0)
Median (IQR)	10.0 (5, 17)
Dose adjusted, n (%)	
No	265 (95.0)
Yes	9 (3.2)
Missing	5 (1.8)

Dosing information not recorded for *5 and †8 patients
IQR, interquartile range; SD, standard deviation; TLV, telavancin

Table 5. Telavancin Dosing Regimen by Baseline Creatinine Clearance

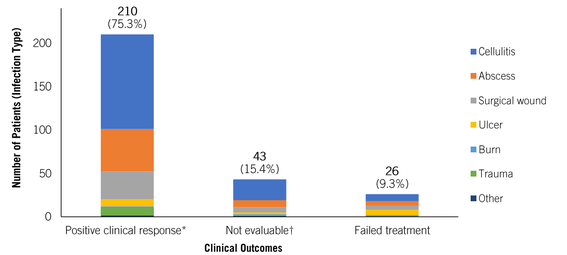
Telavancin Exposure Characteristics	Baseline CrCL (mL/min)*			
	<30 (n = 6)	30–<50 (n = 7)	50–<80 (n = 25)	≥80 (n = 139)
Average daily dose (mg)				
Mean (SD)	555.5 (230.70)	628.6 (118.52)	696.6 (138.38)	829.9 (252.87)
Median (IQR)	650.0 (283.0, 750.0)	600.0 (500.0, 750.0)	750.0 (741.4, 750.0)	750.0 (750.0, 840.0)
Treatment duration (days)				
Mean (SD)	9.3 (4.41)	12.1 (13.43)	11.3 (10.82)	14.0 (11.82)
Median (IQR)	9.0 (5, 12)	5.0 (3, 29)	7.0 (5, 13)	10.0 (6, 19)
Average daily dose (mg/kg)				
Mean (SD)	8.2 (1.68)	9.5 (1.99)	9.6 (2.24)	8.5 (1.95)
Median (IQR)	8.1 (7.2, 9.7)	10.0 (7.2, 10.4)	9.2 (7.7, 10.1)	9.1 (7.2, 10.0)
Dose adjusted, n (%)				
No	6 (100.0)	7 (100)	23 (92.0)	133 (95.7)
Yes	0 (0)	0 (0)	2 (8.0)	6 (4.3)

*Baseline CrCL-based telavancin dosing patterns were not estimated for 102 patients
CrCL, creatinine clearance; IQR, interquartile range; SD, standard deviation

Table 6. Patient Care Setting at Telavancin Initiation

Care Setting	Frequency (%)
Inpatient	56 (20.1)
Hospital floor	46 (16.5)
Intensive care unit	9 (3.2)
Emergency department	1 (0.4)
Outpatient	170 (60.9)
Home	8 (2.9)
Clinic	98 (35.1)
Infusion center	64 (22.9)
Missing	53 (19.0)

Figure 1. Clinical Outcomes at End of Therapy (N = 279)



*Included patients who were cured, had a clinical response within 3–5 days, or were improved to step-down oral therapy
†Included patients for whom outcomes were indeterminate, missing, or undocumented

Table 7. Frequency of Reported Adverse Events of Interest (≥1%)

MedDRA Preferred Term	Frequency (%)
Drug hypersensitivity	3 (1.1)
Nausea	4 (1.4)
Nephrotoxicity* (Nephropathy toxic)	5 (1.8)
Rash	3 (1.1)
Renal failure acute	5 (1.8)

*Prior to amendment 2 of the TOUR protocol, adverse events of interest included nephrotoxicity, infusion reactions, QTc>500 msec, nausea or vomiting of moderate or severe intensity, and hypersensitivity reactions. These reports were before amendment 2 which required a report of a nephrotoxicity adverse event for any change in serum creatinine of ≥0.5 mg/dL or ≥50% regardless of clinical significance or relationship to normal reference range. A patient may have had a 50% increase from baseline in serum creatinine but remained within the normal range
MedDRA, medical dictionary for regulatory activities

CONCLUSIONS

- Telavancin, administered once daily, produced positive clinical outcomes in the majority of patients (210/279, 75.3%) treated for cSSSI
- Telavancin was frequently administered in an outpatient setting, primarily used as a second-line therapy at a median average daily dose of 8.7 mg/kg, median total daily dose of 750 mg, and for a median of 10 days
- The AEs were similar to those reported in previous TLV clinical trials
- These preliminary, real-world data reinforce efficacy results observed in TLV clinical trials and validate ongoing use of TLV for patients with cSSSI (completed TOUR data will be available and reported at a later date)

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