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ORIGINAL RESEARCH ARTICLE

Clinical Experience with Telavancin: Real-World Results from the Telavancin Observational Use Registry (TOUR™)

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Abstract

Background Telavancin—a lipoglycopeptide antibacterial agent active against Gram-positive pathogens including methicillin-sensitive and -resistant *Staphylococcus aureus* (MRSA)—is approved in the USA for once-daily intravenous use. This registry study captured patient characteristics, prescribing patterns, and treatment outcomes associated with telavancin use in real-world clinical practice.

Objective This prospective, multicenter, observational study will characterize current real-world practice patterns for the use of telavancin in the USA by describing demographic and clinical conditions, examining the process of care and rationale for use, and describing the clinical effectiveness and selected safety outcomes among patients treated with telavancin.

Methods The Telavancin Observational Use Registry (TOUR™) is an observational multicenter registry study. Clinical data—including patient demographics, pathogens, telavancin dosing and treatment duration, and adverse events—along with investigators' assessments of outcome, were collected through retrospective medical chart review.

Results Data from 1063 patients were collected from 45 US sites. Of these patients, 29.4% were ≥ 65 years of age [mean age ± standard deviation, 55.2 ± 15.4 years; median age (interquartile range), 57.0 (46.0–66.0)], 53.4% were male, and 83.4% were White. The primary infections in these patients included complicated skin and skin-structure infection (48.7%), bone and joint infections (27.4%), bacteremia and endocarditis (14.2%), and lower respiratory tract infections (8.5%). The predominant pathogen identified was MRSA (37.7%). The mean telavancin dose and duration of treatment were 741.7 ± 194.3 mg and 17 ± 17 days, respectively. Of the 964 (90.7%) patients for whom an end-of-treatment assessment was available, 77.7% had a positive clinical response, 10.1% failed treatment, and 12.2% had indeterminate outcomes.

Conclusions Real-world data collected from the TOUR study show once-daily telavancin is being used for the treatment of a variety of Gram-positive infections with generally positive clinical outcomes.

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Key Points

The Telavancin Observational Use Registry (TOUR™) recorded characteristics and outcomes of telavancin use in clinical practice.

The real-world results from TOUR™ suggest telavancin is a potential treatment option for a variety of infections due to Gram-positive pathogens.

1 Introduction

Gram-positive infections due to *Staphylococcus aureus (S. aureus)* include hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP), complicated skin and skin structure infections (cSSSI), osteomyelitis and septic arthritis, and bacteremia [1]. Serious infections caused by Gram-positive pathogens are commonly treated with glycopeptides, primarily vancomycin, or various β-lactam antibiotics. Estimated glycopeptide use in hospitalized patients in 2012 was greater than penicillin or first-/second-generation cephalosporin but comparable to β-lactam/β-lactamase inhibitor combinations [2]. Vancomycin is often dosed multiple times daily and generally requires therapeutic drug monitoring. However, vancomycin treatment is not always effective; for example, Wunderink reported clinical cure of nosocomial pneumonia following vancomycin treatment in 59/136 patients with *S. aureus* (43.4%) and 22/62 (35.5%) patients with methicillin-resistant *S. aureus* (MRSA) [3]. Furthermore, some *S. aureus* isolates exhibit reduced vancomycin susceptibility [4, 5]. Alternative therapies are needed for challenging *S. aureus* infections.

Telavancin is a once-daily, parenterally administered, optimized lipoglycopeptide antibacterial agent derived from vancomycin, with activity against susceptible Gram-positive pathogens [6]. Telavancin has potent *in vitro* activity against Gram-positive bacteria including methicillin-susceptible *S. aureus* (MSSA), MRSA, vancomycin-intermediate *S. aureus* (VISA), heterogenous VISA, and some *S. aureus* isolates nonsusceptible to linezolid and daptomycin [7–9]. Telavancin has 16- to 32-fold greater activity against MRSA compared with vancomycin [10]. Telavancin demonstrated high cure rates in patients with cSSSI and represents an effective alternative to vancomycin for treatment of monomicrobial *S. aureus* HABP/VABP, especially in patients with complications such as age > 65 years, mechanical ventilation, and isolates with vancomycin minimum inhibitory concentrations ≥ 1 μg/mL [11, 12]. In limited numbers of patients with cSSSI or HABP/VABP with concomitant bacteremia, telavancin efficacy was comparable to vancomycin [13]. Additionally, in randomized controlled trials, telavancin treatment resulted in higher cure and comparable survival rates relative to vancomycin in patients with Gram-positive pneumonia due to *S. aureus* [11, 14].

In the USA, telavancin is approved in adults for treatment of cSSSI caused by susceptible Gram-positive pathogens and for HABP/VABP when alternative treatments are unsuitable [6]. In Canada and Russia, telavancin is approved for treatment of patients with cSSSI and HABP/VABP caused by Gram-positive pathogens [15, 16]. Telavancin is approved in Israel for treatment of adults with nosocomial pneumonia, including ventilator-associated pneumonia, known or suspected to be caused by MRSA, where other alternatives are not suitable [17]. In the EU, telavancin was approved for treatment of nosocomial pneumonia, known or believed to be caused by MRSA, when alternative medicines are unsuitable; however, telavancin was voluntarily withdrawn from the EU market by the sponsor in March 2018 due to limited use of the product [18]. Approved dosing for telavancin for all indications is 10 mg/kg intravenously with adjustments for creatinine clearance (CrCl) described in the product information (PI). The Telavancin Observational Use Registry (TOUR™) was conducted to record population characteristics, prescription information, and real-world clinical outcomes of patients with Gram-positive infections treated with telavancin. Findings from TOUR will improve understanding of US patterns of care for telavancin-treated patients in clinical practice.

2 Methods

2.1 Study Design

TOUR was a multicenter, retrospective, observational registry study conducted at 45 US hospitals or outpatient infusion centers with clinicians routinely involved in care and treatment of bacterial infections between January 2015 and March 2017. The protocol was amended from a prospective to a retrospective design in November 2015; all previously enrolled patients were included. As such, the inclusion/exclusion criteria were limited. At the discretion of the treating physician, any patient who received at least one dose of telavancin as part of clinical care from 1 January 2015 onward was eligible for inclusion in the study. Patients who participated in an interventional research study or clinical trial involving telavancin after 1 January 2015 were excluded. All treatment decisions and clinical assessments were at the treating physician's discretion and not mandated by registry study design or protocol. Data were obtained through retrospective medical chart review; sites were queried after completion of enrollment to resolve missing or unclear entries. Missing data were not imputed. Registry study management performed by Pharmaceutical Product Development, LLC (Wilmington, NC, USA) included recruitment, training, and management of study sites, as well as electronic data capture system and data management. Enrollment was planned for approximately 1000 patients from 50–60 inpatient or outpatient sites that were routinely involved in the treatment of patients with Gram-positive infections.

The registry study was conducted in compliance with the International Society for Pharmacoepidemiology Guidelines for Good Pharmacoepidemiology Practice, the Declaration of Helsinki and its amendments, and the Health Insurance Portability and Accountability Act (HIPAA) of 1996. Institutional Review Board waiver or approval was obtained consistent with local regulations prior to patient data collection at each site. As informed consent was not obtained, only de-identified information was collected in accordance with HIPAA Privacy Rule Section 164.514.

2.2 Patient Populations

Patients who received one or more dose of telavancin on or after 1 January 2015 were eligible for inclusion; individuals who participated in any other telavancin clinical study or trial were excluded. Population size was based on recruitment of patients over a planned period of approximately 3 years.

2.3 Data Collection and Analysis

Data of interest were obtained by medical chart review and entered into electronic case report forms by qualified personnel at each site ≥ 30 days after the last dose of telavancin was administered (see Supplementary Table 1). Clinical responses at end of treatment (EOT) were analyzed in all patients and patients with available assessment at EOT, and categorized as positive, indeterminate due to insufficient information, or failure. Positive clinical responses included patients cured or improved to step-down therapy. Cure was defined as resolution of signs and symptoms of infection and/or no need for additional antibiotic therapy, or clearance of infection as determined by negative culture. Improvement to step-down therapy was defined as partial resolution of clinical signs and symptoms of infection and/or need for additional antibiotic therapy. Failure was defined as inadequate response to therapy, where individuals were resistant to treatment, showed worsening symptoms, or demonstrated new or recurrent signs and symptoms; need to change antibiotic therapy before planned completion of telavancin treatment; or positive culture at EOT.

If a patient died, day of death was recorded as number of days after initiation of telavancin therapy. Renal function was assessed using serum creatinine values obtained ≤ 15 days prior to telavancin therapy (baseline) and at EOT. Use of concomitant antibiotics and potentially nephrotoxic concomitant medications from 2 days prior to telavancin therapy to 2 days after EOT were recorded. Collection of safety data was limited to renal adverse events (AEs), additional AEs leading to discontinuation, and events with fatal outcomes. Renal AEs were defined as any untoward medical occurrence related to the kidney, urinary tract, or renal function per the investigator's discretion. Analysis was performed using SAS® version 9.2 or higher (SAS Institute, Cary, NC, USA). All AE and medical history verbatim terms were recorded and coded using the Medical Dictionary for Regulatory Activities (MedDRA); concomitant medications were coded using the World Health Organization Drug Dictionary. No formal hypothesis or statistical significance testing was planned. Descriptive analyses were performed and reported as mean, median, interquartile range (IQR), number, and proportion of the total population where appropriate.

3 Results

3.1 Patient Disposition, Demographics, Medical History, and Disease Characteristics

TOUR enrolled 1063 patients from 45 US sites (Table 1), of whom 964 (90.7%) had available assessments at EOT and 39/1063 (3.7%) died within 28 days of telavancin initiation; only three deaths were considered possibly treatment related. Disposition of patients with missing or undocumented EOT assessments is summarized in the Supplementary Results. The majority of patients were male (53.4%), White (83.4%), and not Hispanic or Latino (93.5%), with a mean weight of 92.8 ± 24.4 kg and mean body mass index of 31.2 ± 9.5 kg/m^2 (Table 1). Mean patient age was 55.2 ± 15.4 years; 29.4% of patients were ≥ 65 years of age. Of 657 patients with reported baseline CrCl, 13 (2.0%) had CrCl < 30 mL/min and 35 (5.3%) had CrCl 30 to < 50 mL/min; 36 patients were on dialysis. Hypertension (44.8%), diabetes mellitus type 2 (31.5%), and myocardial infarction (10.3%) were the most common baseline co-morbidities (Table 1). Patients were most commonly treated for cSSSI (48.7%), followed by bone and joint infections (27.4%), bacteremia and endocarditis (14.2%), and lower respiratory tract infections (LRTIs; 8.5%).

3.2 Prescribing Patterns

Mean daily dose of telavancin was 741.7 ± 194.3 mg (median 750 mg; IQR 700–750 mg) or 8.4 ± 2.1 mg/kg (median 8.3 mg/kg; IQR 6.9–9.9 mg/kg) (Table 2). The most common average daily dose category was 750 mg in 590 (55.5%) patients, followed by < 750 mg in 290 (27.3%), 1000 mg in 63 (5.9%), > 750 to < 1000 mg in 62 (5.8%), and > 1000 mg in 58 (5.5%) patients. Mean treatment duration was 17 ± 17 days; the most common treatment duration was 7 to < 21 days in 389 (36.6%) patients, followed by < 7 days in 352 (33.1%) patients (Table 2). The mean daily dose of telavancin was lower for patients on dialysis (562.9 ± 255.2 mg) or patients with baseline CrCl < 30 mL/min (513.2 ± 227.6 mg) or 30 to < 50 mL/min

Table 1 Baseline demographics and clinical characteristics

Characteristic	Telavancin ($N=1063$)
Age, years[a]	
Mean (SD)	55.2 (15.4)
Median (IQR)	57.0 (46.0–66.0)
Age category	
< 65 years	749 (70.5)
≥ 65 years	312 (29.4)
Missing	2 (0.2)
Sex	
Male	568 (53.4)
Female	495 (46.6)
Ethnicity	
Hispanic or Latino	25 (2.4)
Not Hispanic or Latino	994 (93.5)
Not reported	25 (2.4)
Unknown	19 (1.8)
Race	
American Indian or Alaska Native	17 (1.6)
Asian	10 (0.9)
Black or African American	126 (11.9)
Native Hawaiian, Pacific Islander, or other	0
White	887 (83.4)
Other	23 (2.2)
BMI, median (IQR), kg/m^2[b]	29.6 (24.7–36.0)
Weight, median (IQR), kg	88.9 (72.0–108.0)
Creatinine clearance, mL/min[c]	
< 30	13 (2.0)
30 to < 50	35 (5.3)
50 to < 80	120 (18.3)
≥ 80	489 (74.4)
Dialysis	36 (3.4)
Intermittent hemodialysis	22 (2.1)
SLEDD	0
CRRT	6 (0.6)
Peritoneal dialysis	1 (0.1)
Missing	7 (0.7)
Co-morbidities present in ≥ 5% of patients	
Hypertension	476 (44.8)
Diabetes mellitus type 2	335 (31.5)
Myocardial infarction	110 (10.3)
Chronic obstructive pulmonary disease	97 (9.1)
Chronic renal failure	88 (8.3)
Cardiac failure congestive	67 (6.3)
Atrial fibrillation	65 (6.1)
Asthma	62 (5.8)
Peripheral vascular disorder	60 (5.6)
Hyperlipidemia	54 (5.1)
Patient care setting at TLV initiation	
Hospital ward	347 (32.6)
Intensive care unit	77 (7.2)
Emergency department	5 (0.5)
Outpatient infusion center	315 (29.6)
Outpatient clinic	283 (26.6)
Other	36 (3.4)

Unless otherwise noted, data presented as *n* (%)

BMI body mass index, *CRRT* continuous renal replacement therapy, *IQR* interquartile range, *SD* standard deviation, *SLEDD* sustained low-efficiency daily dialysis, *TLV* telavancin

[a] $n=1054$; does not include two patients with missing age and seven patients recorded only as ≥ 90 years old

[b] $n=1049$

[c] $n=657$; baseline creatinine clearance data missing for 406 patients

(578.5 ± 169.8 mg) relative to the full population (Table 2). Treatment duration and median average daily dose per body weight were also lower for patients with CrCl 30 to < 50 mL/min relative to the overall population (Table 2), consistent with dose adjustments due to renal impairment as indicated per telavancin labeling [6].

3.3 Pathogens Isolated

Infecting pathogens were identified in 738 (69.4%) patients at baseline (see additional details in the Supplementary Results). Monomicrobial Gram-positive infections were identified in 621 (58.4%) patients, multiple Gram-positive organisms without Gram-negative organisms in 48 (4.5%) patients, and mixed Gram-positive/negative infections in 76 (7.1%) patients. The most common baseline pathogen isolated was MRSA, in 401 (37.7%) patients, followed by MSSA in 119 (11.2%) patients, and coagulase-negative *Staphylococcus* in 93 (8.7%) patients (Table 3).

3.4 Prior Antibiotic Usage

Telavancin was used as first-line therapy in 303 (28.5%) patients and second-line or greater therapy in 760 (71.5%) patients; 519 (48.8%) patients received one prior antibiotic, 188 (17.7%) received more than one, 50 (4.7%) received more than two, and ten (0.9%) received more than three prior antibiotics. The most frequently administered prior antibiotics were vancomycin (29.4%), daptomycin (8.5%), and sulfamethoxazole/trimethoprim (7.8%).

3.5 Clinical Response

Of 964 (90.7%) TOUR patients with available assessment at EOT, 749/964 (77.7%) had positive clinical outcomes, 97/964 (10.1%) patients failed treatment, and 118/964 (12.2%) patients had indeterminate outcomes (Fig. 1). Including all 1063 patients and counting missing

Table 2 Telavancin dosing and treatment duration in patients by baseline renal function

	Baseline CrCl (mL/min)						
	Dialysis ($n=36$)	<30 ($n=13$)	30 to <50 ($n=35$)	50 to <80 ($n=120$)	≥80 ($n=489$)	Missing ($n=370$)	Total ($N=1063$)
Telavancin daily dose, mg							
Mean (SD)	562.9 (255.2)	513.2 (227.6)	578.5 (169.8)	676.7 (142.8)	789.8 (200.8)	740.0 (162.0)	741.7 (194.3)
Median (IQR)	500.0 (341.2–750.0)	500.0 (330.0–650.0)	600.0 (450.0–750.0)	750.0 (540.0–750.0)	750.0 (750.0–750.0)	750.0 (750.0–750.0)	750.0 (700.0–750.0)
Treatment duration, days							
Mean (SD)	16.6 (17.7)	11.2 (12.8)	14.7 (17.9)	14.0 (15.9)	15.5 (17.1)	19.5 (15.6)	16.7 (16.6)
Median (IQR)	10.5 (5.0–25.0)	9.0 (2.0–12.0)	5.0 (2.0–28.0)	8.0 (3.5–16.5)	10.0 (4.0–21.0)	14.0 (7.0–33.0)	10.0 (5.0–26.0)
Treatment duration, days, *n* (%)							
<7	12 (33.3)	5 (38.5)	19 (54.3)	49 (40.8)	175 (35.8)	92 (24.9)	352 (33.1)
7 to <21	14 (38.9)	6 (46.2)	7 (20.0)	44 (36.7)	186 (38.0)	132 (35.7)	389 (36.6)
21 to <35	4 (11.1)	1 (7.7)	3 (8.6)	11 (9.2)	60 (12.3)	57 (15.4)	136 (12.8)
35 to <49	3 (8.3)	0	5 (14.3)	12 (10.0)	56 (11.5)	79 (21.4)	155 (14.6)
≥49	3 (8.3)	1 (7.7)	1 (2.9)	4 (3.3)	12 (2.5)	10 (2.7)	31 (2.9)
Average daily dose per body weight, mg/kg[a]							
Mean (SD)	6.4 (2.5)	7.5 (2.2)	8.0 (2.0)	9.0 (2.0)	8.5 (1.9)	8.2 (2.1)	8.4 (2.1)
Median (IQR)	6.5 (4.4–8.3)	7.2 (6.0–9.2)	7.6 (6.7–9.4)	8.9 (7.6–10.1)	8.6 (7.1–10.0)	8.1 (6.8–9.8)	8.3 (6.9–9.9)
Dose adjusted, *n* (%)							
Yes	3 (8.3)	3 (23.1)	3 (8.6)	15 (12.5)	29 (5.9)	21 (5.7)	74 (7.0)
No	33 (91.7)	10 (76.9)	32 (91.4)	105 (87.5)	460 (94.1)	349 (94.3)	989 (93.0)

CrCl creatinine clearance, *IQR* interquartile range, *SD* standard deviation

[a]Total, $n=1054$; missing, $n=361$

Table 3 Pathogens for which telavancin is indicated present at baseline in ≥1% of patients

Pathogen	Telavancin ($N=1063$)
MRSA	401 (37.7)
MSSA	119 (11.2)
Coagulase-negative *Staphylococcus*	93 (8.7)
Enterococcus faecalis	28 (2.6)
Group B *Streptococcus*	20 (1.9)
Enterococcus faecium	13 (1.2)

Data presented as *n* (%)

MRSA methicillin-resistant *Staphylococcus aureus*, *MSSA* methicillin-sensitive *Staphylococcus aureus*

assessments at EOT as failures, 70.5% had a positive clinical response, 18.4% failed treatment (9.1% with documented treatment failure and 9.3% with missing or undocumented assessment), and 11.1% had indeterminate outcomes. Among patients with available EOT assessment, the overall positive clinical response rates by infection type were comparable at 74.2% in patients with bacteremia or endocarditis, 78.7% in patients with bone and joint infections, 80.1% in patients with cSSSI, and 67.1% in patients with LRTI (Fig. 1); however, these groups were not mutually exclusive or comprehensive. Outcomes by cSSSI and LRTI subtype are reported in the Supplementary Results. The positive clinical response rate was 78.8% for all infections with Gram-positive pathogens, 76.2% for MRSA, 80.7% for MSSA, 86.0% for multiple Gram-positive infecting pathogens, and 58.5% for mixed Gram-positive and Gram-negative infections. At post-treatment assessment, recurrence of infection or reinfection occurred in 19/809 patients assessed. Available data for 99 patients without EOT assessments is presented in the Supplementary Results and Supplementary Table 2; reasons for missing or undocumented assessments were not captured.

3.6 Location of Care and Care Setting Utilization

The majority of patients, 598/1063 (56.3%), were treated in outpatient infusion centers or clinics. A total of 429/1063 (40.4%) initiated telavancin treatment as inpatients [77 (7.2%) in an intensive care unit (ICU), 347 (32.6%) in other hospital settings, and 5/1063 (0.5%) in an emergency department].

For patients who initiated telavancin treatment in non-ICU hospital settings, the mean duration of hospitalization was 12.8 ± 14.5 days (range 1–94 days). For patients who started treatment in the ICU, the mean duration of

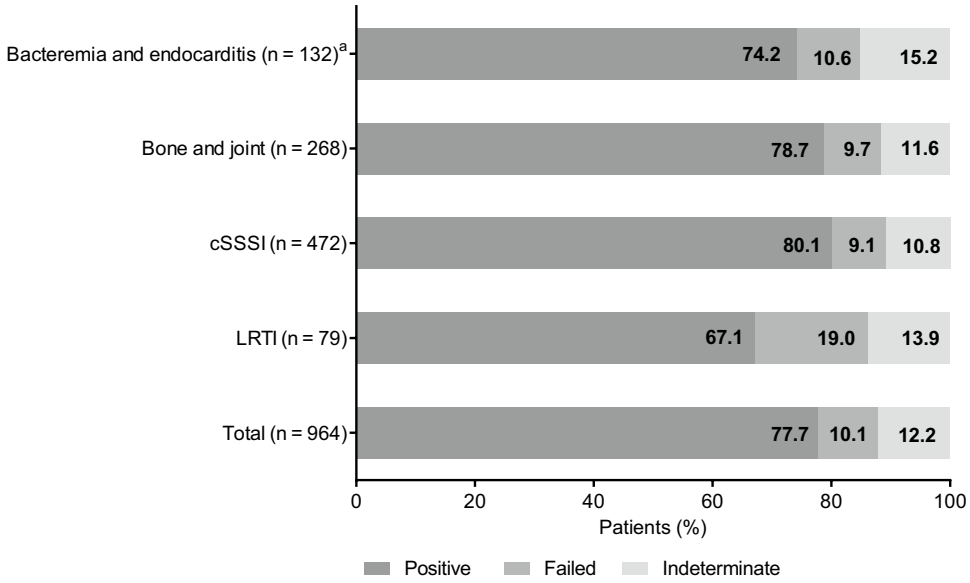

Fig. 1 Clinical outcomes for TOUR patients available for assessment at the end of treatment for major infection types. [a]The represented groups are not mutually exclusive, and not comprehensive. Positive clinical response includes cured and improved to step-down oral therapy. *cSSSI* complicated skin and skin-structure infections, *LRTI* lower respiratory tract infection, *TOUR* Telavancin Observational Use Registry

stay was 30.1 ± 45.4 days. Mean treatment durations in outpatient infusion centers or clinics were 20.8 ± 19.3 and 17.6 ± 15.8 days, respectively. Mean duration of treatment initiated in other locations, such as home, was 32.3 ± 15.5 days.

3.7 Safety

Treatment-emergent AEs (TEAEs) of interest comprised renal TEAEs in 63 (5.9%) patients, including renal failure in 62 (5.8%) patients; TEAEs leading to discontinuation of telavancin in 122 (11.5%) patients; and TEAEs leading to fatal outcomes in 31 (2.9%) patients (Table 4). Serious TEAEs occurred in 44 (4.1%) patients; of these patients, 24 (2.3%) discontinued the registry study. The 31 fatal TEAEs included three deaths possibly related to telavancin and two deaths for which relationship to treatment was not recorded; the remaining fatal TEAEs were judged unrelated to telavancin. The most common TEAEs were renal failure (62/1063; 5.8%), nausea (18/1063; 1.7%), and vomiting (11/1063; 1.0%) (Table 4). Renal failure was considered possibly related to treatment in 58 (5.5%) patients and resulted in telavancin discontinuation in 37 (3.5%) patients (Table 2). Dialysis was recorded as an intervention in 11 (1.0%) patients. Renal failure resolved in 46 (4.3%) patients and led to a fatal outcome in one (0.1%) patient (Table 2). Serious renal TEAEs occurred in 15 (1.4%) patients and were considered possibly related to telavancin in 13/15 patients. Although not reported as serious AEs, nausea and vomiting were reported as possibly related to treatment in 18 (1.7%) and 11 (1.0%) patients, respectively; these events all led to discontinued treatment but eventually resolved in all patients.

Baseline and post-baseline creatinine measurements were available for approximately 43% of patients and remained generally stable throughout treatment. Change in mean serum creatinine measurements was small, from 0.96 mg/dL at baseline to 1.07 mg/dL at EOT. Likewise, mean CrCl was 127.31 mL/min at baseline and 113.72 mL/min at EOT. Among 63 patients with renal AEs, 48 (76%) received vancomycin < 2 days prior to telavancin or were taking other nephrotoxic medications concomitantly, as did 4/7 patients investigated for potentially reduced renal function. Concomitant administration of nephrotoxic medications, most commonly acetylsalicylic acid (17.8%), lisinopril (14.3%), and vancomycin (14.3%), was recorded in 349 patients. Piperacillin sodium with tazobactam was administered before telavancin in three (0.9%) patients. As vancomycin and telavancin should not be administered together, recorded concomitant vancomycin use may represent instances where the last dose of vancomycin was administered < 2 days prior to the first dose of telavancin during antibiotic switching (Supplementary Table 3).

4 Discussion

Real-world treatment results from TOUR support the use of telavancin for a variety of infections due to Gram-positive pathogens. Telavancin treatment produced positive clinical responses in the majority of patients assessed at EOT when used for the approved indications of cSSSI and HABP/VABP. Positive clinical responses also resulted from telavancin treatment for other LRTIs, bacteremia and endocarditis, or bone and joint infections. Patients were treated in a range of care settings for a typical duration of 7–21 days at a median telavancin dose of 8.3 mg/

Table 4 Treatment-emergent adverse events (≥ two patients)

MedDRA preferred term	Frequency	Serious	Possibly related to treatment	Discontinued treatment[a]	Resolved[b]	Fatal[c]
Any TEAE	155 (14.6)	44 (4.1)	119 (11.2)	122 (11.5)	113 (10.6)	31 (2.9)
Renal failure[d]	62 (5.8)	15 (1.4)	58 (5.5)	37 (3.5)	46 (4.3)	1 (0.1)
Nausea	18 (1.7)	0	18 (1.7)	18 (1.7)	18 (1.7)	0
Vomiting	11 (1.0)	0	11 (1.0)	11 (1.0)	11 (1.0)	0
Respiratory failure	7 (0.7)	7 (0.7)	0	7 (0.7)	0	7 (0.7)
Blood creatinine increased	6 (0.6)	0	6 (0.6)	4 (0.4)	6 (0.6)	0
Cardiac arrest	6 (0.6)	6 (0.6)	1 (0.1)	6 (0.6)	0	6 (0.6)
Drug intolerance	6 (0.6)	0	6 (0.6)	6 (0.6)	6 (0.6)	0
Rash	6 (0.6)	0	6 (0.6)	6 (0.6)	6 (0.6)	0
Drug hypersensitivity	4 (0.4)	0	4 (0.4)	4 (0.4)	4 (0.4)	0
Hypersensitivity	4 (0.4)	0	4 (0.4)	4 (0.4)	4 (0.4)	0
Septic shock	4 (0.4)	4 (0.4)	1 (0.1)	3 (0.3)	0	4 (0.4)
Death[e]	3 (0.3)	3 (0.3)	0	2 (0.2)	0	3 (0.3)
Sepsis	3 (0.3)	3 (0.3)	1 (0.1)	3 (0.3)	0	3 (0.3)
Cardiac failure congestive	2 (0.2)	2 (0.2)	0	0	0	2 (0.2)
Dysgeusia	2 (0.2)	0	2 (0.2)	2 (0.2)	2 (0.2)	0
Dyspnea	2 (0.2)	0	0	2 (0.2)	2 (0.2)	0
Infusion-related reaction	2 (0.2)	0	2 (0.2)	2 (0.2)	2 (0.2)	0
Osteomyelitis	2 (0.2)	0	0	2 (0.2)	2 (0.2)	0
Pyrexia	2 (0.2)	0	1 (0.1)	2 (0.2)	2 (0.2)	0

Data presented as *n* (%)

MedDRA Medical Dictionary for Regulatory Activities, *TEAE* treatment-emergent adverse event

[a]"Discontinued" treatment includes those patients who had drug withdrawn or who withdrew from the study

[b]"Resolved" includes those events that were recovered/resolved, recovered/resolved with sequelae, or recovering/resolving

[c]Fatal TEAEs were considered related to telavancin treatment in three patients, including one event each of cardiac arrest, septic shock, and sepsis. The relationship to treatment was not recorded in 2 patients. The remaining fatal TEAEs were considered unrelated to telavancin treatment

[d]"Renal failure" includes the addition of values reported for "renal failure" and "renal failure acute" preferred terms, as defined by MedDRA

[e]Reason unknown

kg (IQR 6.9–9.9 mg/kg). Despite real-world use of telavancin at lower doses relative to labeling (10 mg/kg) [6], patients showed mostly positive clinical responses to treatment. Telavancin was generally well tolerated. Patients enrolled in TOUR had varying levels of renal function at baseline and were dosed accordingly. Following telavancin treatment, 62 patients (5.8%) experienced renal failure, which resolved in 46/62 patients (74.2%). Among patients who experienced renal AEs, 48/63 (76%) received other nephrotoxic medications ≤ 2 days before or during telavancin therapy, which may have contributed. These included patients who received vancomycin, which has been associated with renal toxicity in similar patients [19, 20]. Overall, telavancin produced positive clinical outcomes in at least 70% of patients and was generally well tolerated.

In phase 3 trials, telavancin was a noninferior alternative to vancomycin for the approved indications of cSSSI and HABP/VABP infections due to MRSA and MSSA. For some infections, especially cSSSI caused by MRSA and HABP/VABP due to *S. aureus* with a vancomycin minimum inhibitory concentration ≥ 1 µg/mL, clinical cure rates were numerically higher in patients treated with telavancin versus vancomycin [11, 12, 21]. In a retrospective analysis of the phase 3 trials, telavancin also demonstrated noninferiority to vancomycin for treatment of cSSSI and HABP/VABP with concomitant bacteremia [13]. In other studies, telavancin therapy had comparable efficacy to standard treatment (vancomycin or anti-staphylococcal penicillin) for *S. aureus* bacteremia [22] and achieved clinical success in 7/8 patients with end-stage renal disease with MRSA bacteremia who failed treatment with other therapies [23] and 10/14

patients with MRSA bone and joint infections [24]. Results from TOUR confirm the real-world efficacy of telavancin for treatment of the approved indications and provide evidence that clinicians are successfully using telavancin to treat additional infection types.

This registry study has several limitations inherent to observational studies including being neither controlled nor blinded. Patient enrollment decisions were made by individual clinicians, potentially biasing patient selection. All data were gathered from retrospective medical chart review, limiting available information. Efficacy outcomes were based on subjective assessments of investigators at each site, thus individual interpretation could introduce bias. Additionally, patient loss to follow-up may have impacted interpretation. The microbiology data can only be considered supportive due to differing standards of care and nonsystematic collection of microbiology data across participating sites. Collection of TEAEs was limited to events of interest, and renal function results were not collected systematically. Despite these limitations, TOUR includes a large cohort of patients with a wide range of clinical characteristics and infection types and provides data on real-world use of telavancin.

5 Conclusion

Overall, TOUR documents telavancin use in clinical practice with satisfactory results. While prescribers should continue to monitor renal function closely, this registry provides data on the impact of renal toxicity in real-world prescribing. Data from TOUR supports use of telavancin for the approved indications of cSSSI and HABP/VABP while providing insight into clinician use of telavancin for additional infection types, including other LRTIs, bacteremia and endocarditis, and bone and joint infections.

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Compliance with Ethical Standards

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Conflict of interest Dr. Bressler has received fees for participating in advisory boards and speaker bureaus for the Theravance Biopharma group of companies. Dr. Hassoun has received fees for participating in advisory boards and speaker bureaus for the Theravance Biopharma group of companies. Dr. Saravolatz has previously received fees for participating in advisory boards and speaker bureaus for the Theravance Biopharma group of companies; and he has received research grants from Theravance Biopharma US, Inc., paid to Saint John Hospital and Medical Center during the course of the study. Dr. Ravenna is an employee of Theravance Biopharma US, Inc., and holds stock in Theravance Biopharma, Inc. Dr. Castaneda-Ruiz and Dr. Barnes are former employees of Theravance Biopharma US, Inc., and hold stock in Theravance Biopharma, Inc.

Data availability Theravance Biopharma, Inc. (and its affiliates) will not be sharing individual de-identified participant data or other relevant study documents.

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