IDSA 2011 #307

Infectious Disease Specialists of Atlanta

HEALIX

Outpatient Parenteral Antibiotic Therapy (OPAT) with Telavancin: A Multi-Center Experience

Robin H. Dretler, MD[1], John S. Adams, MD[2], Michael P. Dailey, MD[3], Lucinda J. Van Anglen, PharmD[4]

[1]Infectious Disease Specialists of Atlanta, Atlanta, GA, [2]Knoxville Infectious Disease Consultants, PC, Knoxville, TN, [3]Infectious Disease Services of Georgia, Roswell, GA, [4]Healix Infusion Therapy, Inc., Sugar Land, TX

Lucinda J. Van Anglen, PharmD
Healix Infusion Therapy
14140 SW Fwy, 4th Floor
Sugar Land, TX 77478
281-295-4000
Lvananglen@healix.net

Abstract

Background: Telavancin (TLV) is a novel lipoglycopeptide FDA approved September 2009 for the treatment of acute bacterial skin and skin structure infections (SSI) caused by susceptible gram positive bacteria. To date, there is little data regarding OPAT use of TLV. A physician office infusion center (POIC) provides an optimal outpatient setting for the treatment of SSI and other serious infections caused by gram positive bacteria. This study's purpose was to evaluate all uses, on- and off-label, therapy characteristics and outcomes of patients (pts) receiving OPAT with TLV in POICs. **Methods:** A retrospective database and chart review of 15 POICs was conducted to identify all pts receiving TLV from November 1st, 2009 through December 31, 2010 for OPAT therapy. Patient demographics, diagnosis, therapy characteristics, adverse events (AEs) and primary outcomes were evaluated. **Results:** 47 pts met inclusion criteria. Pts were treated for SSI (24, 51%), osteomyelitis (OM), (19, 40%), sepsis (S), (3, 6%) and pneumonia (P), (1, 2%). Mean age was 56 yrs with 49% males. Common comorbidities were hypertension (19, 40%) and diabetes (18, 38%). The most prevalent pathogen reported was MRSA (22, 47%). Mean duration of therapy was 25 days (SSI-14, OM-38, P-36, S-19). Outcome was evaluated in 39/47 pts. Cure was reported in 17/39 (44%), improvement in 11 (28%), failure in 11 (28%). Outcomes in SSI were cure in 6/17 (35%), improving in 6 (35%), failure in 5 (29%) with 4 due to an AE. Outcomes in OM were cure in 7/18 (39%), improving in 5 (28%), failure in 6 (33%) with 3 due to an AE. The P patient was cured (100%) and the 3 pts with sepsis were cured (100%). Overall, AEs occurred in 24 pts (51%). Serious adverse events occurred in 5 (8%) and included hematologic changes (3), nephrotoxicity (1), and bradycardia with QT prolongation (1). Treatment discontinuations due to adverse events occurred in 8 pts (17%) due to severe nausea (4-SSI), rash (1-SSI, 1-OM), hematologic changes (1-OM), nephrotoxicity (1-SSI) and QT prolongation (1-OM). **Conclusion:** TLV therapy may be successful in treatment of SSI and additional off-labeled diagnoses in the OPAT setting but AE and discontinuation rates were notable. Additional prospective studies are warranted.

Introduction

Telavancin received FDA approval in late 2009 for the treatment of complicated skin and skin structure infections. Telavancin is a novel lipoglycopeptide and a semi-synthetic derivative of vancomycin, a glycopeptide. It exerts rapid concentration-dependent bactericidal effects and, like vancomycin, inhibits bacterial cell wall synthesis. Unlike vancomycin, telavancin employs a unique dual mechanism of action, disrupting bacterial membrane's functional integrity and also binding to bacterial membrane.[1,2] Methicillin-resistant *S. aureus* (MRSA) is both nosocomial and community-acquired, with mortality rates estimated at 20% in the United States. Therefore, empiric coverage for MRSA infections should be considered when choosing a treatment regimen. According to the most recent guidelines, telavancin is now an A-1 recommendation for intravenous treatment of complicated SSI.[3] Telavancin, unlike vancomycin, is dosed daily and, therefore, may be advantageous for use in the outpatient treatment setting. POICs provide an outpatient treatment setting for patients requiring intravenous antibiotics (IVAB) for the treatment of serious infections, including SSI. The study purpose was to evaluate use and outcomes of patients treated in POICs with telavancin.

Methods

We retrospectively queried our database of 57 ID POICs to identify all pts receiving OPAT TLV from November 1st, 2009 through December 31, 2010. Subsequently, charts were reviewed for patient demographics, diagnosis, therapy characteristics, adverse events (AEs) and outcomes. Patients were excluded for age less than 18 years.

Data Analysis

- Outcomes were evaluated as "cured" or as "improving or resolving", both indicating no remaining evidence of infection, or as failed. Clinical success was identified as those cured or resolved.
- Creatinine clearance (CrCl) was calculated according to Cockcroft-Gault formula.
- Descriptive statistics (mean, standard deviation) were used for demographic data.
- Percentages were used for safety and efficacy data.

Results

Demographics

Table 1. Demographics n=47

Characteristic	No. (%)
Female gender	24 (51)
Child bearing age (<40)	2 (4)
Age in yrs, Mean (Range)	56 (18-94)
≤ 64	33 (70)
65 - 80	11 (24)
≥81	3 (6)
Creatinine clearance < 30 (ml/min)	1 (2)
Comorbidities	
Hypertension	19 (40)
Diabetes mellitus	18 (38)
Dyslipidemia	11 (23)
GERD	9 (19)
COPD/Asthma/Emphysema	5 (11)
Coronary artery disease	5 (11)
Neuropathy	5 (11)
Chronic kidney disease	3 (6)
Other reported comorbidities	38 (19)
Comorbidities per patient	
None	8 (17)
One	6 (13)
Two	7 (15)
Three or more	26 (55)

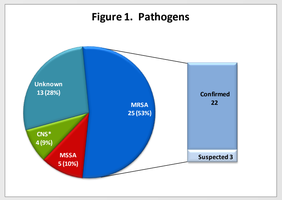
Table 2. Diagnoses Treated

Diagnosis	No. (%)
Acute Bacterial SSI	24 (51)
Osteomyelitis	19 (41)
Sepsis	3 (6)
Pneumonia	1 (2)

- 47 patients received telavancin at 15 POICs in the 16 month period
- Patients were relatively young with 70% less than 64 years
- Multiple comorbidities were common with three or more in 55% of pts
- Majority of use was in SSI, but 40% of pts were treated for osteomyelitis

Pathogen

Figure 1. Pathogens

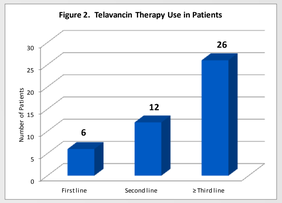


*CNS=Coagulase negative staphylococcus

- MRSA was the most common infecting organism (53% overall, including suspected cases)

Place in therapy

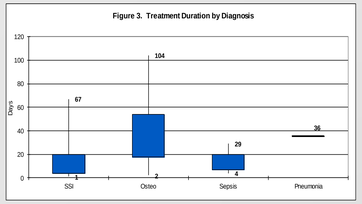
Figure 2. Telavancin Therapy Use in Patients



- 6 patients (4 osteomyelitis and 2 cellulitis) received TLV as first line therapy
- 24 patients received vancomycin and 16 patients received daptomycin prior to treatment with TLV
- 10 patients received a trial of oral antibiotics prior to treatment initiation with TLV
- 3 pts were non-evaluable for place in therapy

Treatment

Figure 3. Treatment Duration by Diagnosis



- Total mean duration of therapy was 25 days (1-104)
  - One pt received 104 days of tx for osteo without adverse events
- Mean therapy duration of telavancin therapy for cellulitis (14), osteomyelitis (38), sepsis (19) and pneumonia (36) varied between diagnoses
- Mean telavancin dose was 10mg/kg for all pts
  - Mean dose by diagnosis was 9.25 mg/kg (SSI), 9.3 mg/kg (osteo), 11 mg/kg (sepsis) and 8 mg/kg (pneumonia)

Table 3. Concomitant Therapies

Drug	n=11
Ceftriaxone	4
Cefepime	3
Micafungin	2
Aztreonam	1
Clindamycin	1
Fluconazole	1
Meropenem	1
Rifampin IV	1
Amoxicillin PO	1
SMZ-TMP PO	1
Rifampin PO	1

- 11 patients (23%) received concomitant therapy with telavancin
- 4 patients (8%) received >1 additional therapy with telavancin

Safety

Table 4. Frequency of Adverse Events Related to Telavancin

System Organ Class and Preferred Term	Age ≤ 64 No. (%)	Age 65 - 80 No. (%)	Age ≥ 81 No. (%)
Blood disorders	4		
Leukopenia	1 (2.2)		
Anemia	1 (2.2)		
Neutropenia	1 (2.2)		
Thrombocytopenia	1 (2.2)		
Gastrointestinal disorders	15	6	
Nausea	7 (15.9)	2 (4.5)	
Vomiting	2 (4.5)	3 (6.8)	
Taste disturbance	6 (13.6)	1 (2.2)	
Cardiac disorders	2		
Bradycardia, QT prolongation	1 (2.2)		
Chest pressure	1 (2.2)		
Infections		1	
Vaginal yeast infection		1 (2.2)	
Renal and urinary disorders	5		1
Nephrotoxicity	1 (2.2)		
Foamy urine	4 (9.1)		1 (2.2)
Skin disorders	3		
Itching	2 (4.5)		
Rash	1 (2.2)		
General disorders	6	1	
Fatigue	2 (4.5)	1 (2.2)	
Fever	1 (2.2)		
Chills	1 (2.2)		
Coughing	1 (2.2)		
Bone pain	1 (2.2)		
Total Treatment-related Adverse Events	35	8	1

- 24 of 47 (51%) of patients experienced a total of 44 adverse events
- The majority of AEs occurred in the lowest age group (≤64)
- AEs occurred most often as gastrointestinal disorders with nausea, 9 (20% of all AEs), taste disturbance, 7 (16% of AEs) and vomiting, 5 (11%)

Safety, cont.

Table 5. Adverse Events Requiring Interventions

Pt. Number	Adverse Event	Intervention	Age	Diagnosis	TLV treatment duration (days)	TLV dose (mg/kg)	Comorbidities
Serious AEs							
1	SCr rise, fever, chills, itching, bone pain	Drug discontinuation, admitted to hospital	61	cellulitis	14	5.8	DM, GERD, HTN, history of MI, neuropathy, gallbladder disease, morbid obesity
2	Bradycardia, QT prolongation, taste disturbance, foamy urine	Drug discontinuation	60	osteo	50	7.5	Renal cancer, prior nephrectomy, obese
3	Pancytopenia	Drug discontinuation, therapy changed	46	osteo	12.5	10	none
4	Severe anemia	Transfusion, therapy complete	47	sepsis	29	11.9	Immune deficiency, telangiectasia, obese
Mild to Moderate AEs							
5	N/V, taste disturbance, foamy urine	Drug discontinuation, therapy complete	60	cellulitis	20	8.9	DM, dyslipidemia, HTN, CAD, CABG, obese
6	Severe nausea, taste disturbance	Drug discontinuation, therapy changed	36	cellulitis	2	10	obese, DM, dyslipidemia, GERD, HTN, anxiety, peripheral neuropathy
7	Severe nausea	Drug discontinuation, therapy changed	54	cellulitis	4	10.3	DM, dyslipidemia, GERD, HTN, peripheral neuropathy, obese
8	Itching, severe HA, coughing	Drug discontinuation	52	cellulitis	1	10.2	DM, COPD, GERD, obese
9	Nausea, vomiting, fatigue	Drug discontinuation, therapy changed	69	cellulitis	3	9.8	DM, dyslipidemia, HTN, obese
10	Taste disturbance	Dose decreased	65	osteo	41	7.5	HTN, RA, nephrectomy, CHF, GERD, RBBB
11	Foamy urine, hx of drug allergies	Diphenhydramine added	49	osteo	15	10	none

- 11 patients overall (23%) experienced an AE which required intervention

Serious AEs

- 3 of the 4 pts with serious AEs had symptom resolution upon discontinuation of TLV
- 1 patient expired after a complicated hospital admission
- Mean therapy duration was 27 days

Mild to Moderate AEs

- 5 of the 7 patients discontinued TLV as a result of the adverse event
- Diphenhydramine allowed 1 patient to continue on TLV treatment

Outcomes

Figure 4. Outcomes by Diagnosis

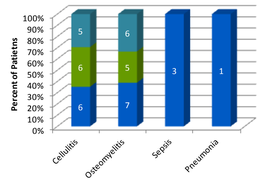
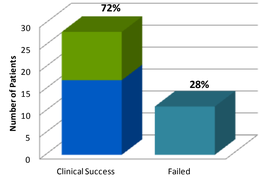


Figure 5. Overall Therapy Outcome



- 39/47 pts were evaluable for clinical outcomes
- 72% of patients had overall clinical treatment success, defined as cured or resolving, with no remaining evidence of infection
- Success rate was 70% for SSI, 67% for osteomyelitis, 100% for sepsis and 100% for pneumonia
- Failures were primarily AE related, 7 of 11 patients (64%)

Discussion

- Daily dosing and effectiveness in treating MRSA makes telavancin advantageous for use in the OPAT setting.
- Telavancin demonstrated an overall clinical success rate (cured plus resolving) of 70%for treatment of acute bacterial skin and skin structure infections.
- Additional use of telavancin was noted effective in treatment of:
  - osteomyelitis (67% clinical success)
  - sepsis (100% cure)
  - pneumonia (100% cure).
- Telavancin was used primarily as a 3rd line or higher agent (60%). Second line therapy accounted for 27% and 1st line therapy for 13%.
- Primary pathogen treated with telavancin was MRSA (53%).
- Mean duration of therapy was 25 days;, which was higher than previously studied.
- Adverse events were frequent (51%) in our patient population. Intervention was required in 23% of patients overall. Clinical failures due to adverse events was noted in 18% of evaluable patients.
- Adverse event rates could be related to the number of comorbidities which were high in the entire study population. Extended duration of therapy may have also contributed in some adverse events.

Conclusions

- Telavancin was effective in treatment of complicated skin and skin structure infections, osteomyelitis, sepsis and pneumonia.
- Telavancin may be a valid first line treatment option in patients without serious comorbidities.
- Management of adverse events must be considered with telavancin therapy.
- Further investigation is needed to ascertain the ideal patient population.

References

1. Saraf, LJ, et al. Telavancin, a new lipoglycopeptide antimicrobial, in complicated skin and soft tissue infections. Infection and Drug Resistance 2011;4:87-95.
2. Yin, LY, et al. Efficacy of telavancin in the treatment of methicillin-resistant Staphylococcus aureus osteomyelitis: studies with a rabbit model. J Antimicrob Chemother 2009;63:357-360.
3. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children: executive summary. Clinical Infectious Diseases 2011;52(3);285-292.