POSTER# 688

ADMISSION RATE AND LENGTH OF STAY FOR SKIN INFECTION PATIENTS IN US HOSPITALS: USE OF ORITAVANCIN IS ASSOCIATED WITH LOWER RATES OF HOSPITAL ADMISSION AND SHORTER LENGTH OF STAY

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ABSTRACT

Introduction: When single-dose oritavancin was introduced in 2014 for the treatment of acute bacterial skin and skin structure infection, it was hypothesized that its single-dose formulation may help US hospitals reduce use of inpatient beds through treatment entirely in the outpatient setting and reduction in length of stay (LOS) for admitted patients. This analysis sought to assess the real world impact of oritavancin to US hospitals.

Methods: Data were extracted from the Premier Hospital Database for the first full year of oritavancin availability (2015). Hospital admission rates and LOS were assessed for patients receiving oritavancin for skin infection and compared with patients receiving any other intravenous (IV) antibiotic grouped by infection severity (no systemic symptoms, with systemic symptoms, life-threatening infection) and presence of comorbid conditions using Charlson Comorbidity Index score (CCI).

Results: There were 208,113 records for patients 18+ with a primary diagnosis of skin infection and administration of IV antibiotic. Among 203 patients who received oritavancin, the average CCI was 1.46; 24.1% patients CCI ≥3; 9.8% life-threatening condition (4.4%) or systemic symptoms (5.4%). 144 (70.9%) oritavancin patients were treated as outpatients. For the 59 patients who were hospitalized (LOS=4.0d), 56 patients received oritavancin after the discharge of hospitalization or at discharge. Compared to patients receiving other IV antibiotics, the patients who received oritavancin had consistently lower admission rates (rate reduction up to 45.4%) across all levels of infection severity and CCI. If admitted, oritavancin patients had shorter LOS (LOS reduction up to 1.8 days) across all severity levels except CCI=1 group.

Conclusion: This analysis finds that use of oritavancin avoided hospitalization and shortened length of stay for skin infection patients. As skin infections represent 2% of all US hospital admissions, increased use of oritavancin may represent an opportunity to recover several hundred thousand bed days for use with other patients.

INTRODUCTION

- Skin and soft tissue infections (SSTI) represent an unrecognized burden to the healthcare system in the United States (US). There were 3.4 million emergency department visits for SSTI in 2011.[1] While the majority of SSTI can be effectively treated with oral antibiotics, the more severe of these, acute bacterial skin and skin structure infections (ABSSSI), require IV antibiotic therapy. As a result, twenty percent of SSTI patients are hospitalized[2,3], making SSTI the cause of 2% of all hospital admissions at a cost to hospitals of $7000-$10,000 per admission.[4,5]
- Even though outpatient parenteral antibiotic therapy (OPAT) has demonstrated the potential to reduce costs and improve patient satisfaction through avoidance of hospital admission for appropriate patients, the most frequently used intravenous (IV) antibiotics, vancomycin and daptomycin, require 7 to 14 days of therapy. Thus treatment completion has involved multiple visits and extensive patient and physician time commitment.
- Approved in 2014, once-only oritavancin facilitates treatment of many ABSSSI patients in the outpatient setting by providing a full course of therapy in one dose. It was hypothesized that its single-dose formulation may help US hospitals reduce use of inpatient beds through treatment entirely in the outpatient setting and reduction in length of stay (LOS) for admitted patients. This analysis sought to assess the real world impact of oritavancin to US hospitals.

METHODS

Study Design

- Retrospective, observational study.

Data Sources

- Data was extracted from the Premier hospital database, one of the largest US hospital clinical and economic databases. It contains data from more than 500 hospitals, representing all geographical areas, a broad range of bed sizes, and teaching, nonteaching, urban, and rural facilities. In addition, the Premier hospital database also contains all patient-level, day-of-service billed items, including procedures, medications, laboratory, and diagnostic and therapeutic services delivered within the hospital.

Study Population

- During development of the original abstract, only the first full year (2015) of oritavancin data was available from Premier database. Since abstract approval, two additional quarters of data became available. The study population in this poster consisted of all adult patients who were treated for SSTI and received single-dose oritavancin, twice-daily vancomycin, or once-daily daptomycin, at either inpatient or outpatient setting of acute care hospitals between January 01, 2015 to June 30, 2016.
- Vancomycin and daptomycin were chosen as the comparators since vancomycin, as the most frequently used IV antibiotic for skin infection (>64%), was often considered as the standard of care for SSTI7 and daptomycin, due to the advantage of once-daily dosing schedule and reduced monitoring, became a more popular newcomer to the gram-positive antimicrobial arsenal.
- SSTI was defined as either one of primary diagnoses of
  - Cellulitis/abscess of ICD-9-CM codes 035, 681.00, 681.10, 681.9, and 682 (ICD-10-CM codes of A46, L02, and L03),
  - Wound infection of ICD-9-CM codes 958.3 and 998.5 (ICD-10-CM codes of T81.4)
  - Other unspecified skin infection of ICD-9-CM codes 686.8 and 686.9 (ICD-10-CM codes of L08.8 and L08.9)

Statistical Analysis

- Data elements used in this analysis included patient demographic characteristics, presence of comorbid conditions (Charlson Comorbidity Index [CCI]), infection severity (no systemic symptoms, with systemic symptoms, life-threatening infection), and hospital admission rates and LOS.
- The designation of life- and non-life-threatening infections was based on Eron classification6 and clinical algorithms:
  - Life-threatening condition included necrotizing fasciitis/limb-threatening infections due to vascular compromise, bacteremia, neutropenia, sepsis and systemic inflammatory response syndrome (SIRS).
  - Systemic symptoms but non-life threatening condition included presence of individual systemic symptoms of hypotension, mental status change, tachycardia, tachypnea, acute kidney failure, renal failure, fever or abnormal glucose.
- As patients frequently received more than one antibiotic during treatment, treatment assignment was in priority from highest to lowest: oritavancin, daptomycin and vancomycin. A descriptive analysis was used to characterize SSTI patients who received oritavancin and to compare with patients who received either daptomycin or vancomycin. Descriptive statistics for continuous variables included means and standard deviations (SD). Categorical variables were summarized by frequencies and percentages. Due to the descriptive and exploratory nature of this study, no formal hypothesis testing was conducted and no inferential statistics was produced.
- Data processing, summarization and analyses were performed using SAS Version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

- **Among 163,731 records for patients 18+ with a primary diagnosis of skin infection and administration of IV antibiotics, vancomycin was the most frequently used agent (n=154,384), followed by daptomycin (n=8,941). 406 patients received oritavancin from 53 hospitals.**

Oritavancin patient profile and treatment pathway

- The average CCI score was 1.5; 53.0% patients had at least one comorbidity; 21.9% patients had CCI ≥3; 12.3% and 28.3% patients had diabetes with or without complications respectively (**Table 1**).
- 127 (31.3%) out of 406 oritavancin-treated patients were hospitalized.
  - The admission rates were consistently lower across all levels of infection severity and CCI, compared to patients receiving daptomycin and vancomycin (**Figure 1**). If admitted, oritavancin patients had shorter LOS across all severity levels except CCI=1 group, compared to patients receiving daptomycin and vancomycin (**Figure 2**).
  - 116 (91.3%) patients received oritavancin either after hospital discharge (n=63), on the day of discharge (n=33), or one day before discharge (n=20).
  - Prior to oritavancin administration, 78 patients were treated with vancomycin and 15 patients with daptomycin.
- 279 (68.7%) out of 406 oritavancin-treated patients were treated completely in an outpatient setting.
  - Compared to patients who were treated with vancomycin at outpatient setting, the oritavancin-treated patients were older and tended to have more comorbidities, particularly diabetes with complication. Oritavancin was more often given to outpatients who had renal disease (**Table 2**).

TABLE 1. DEMOGRAPHIC CHARACTERISTICS AND INFECTION SEVERITY

	Oritavancin (N=406)	Daptomycin (N=8,941)	Vancomycin (N=154,384)
Age (years)	54.2±17.3	55.5±16.9	54.7±18.2
Age ≥ 65 years old, %	29.1%	32.4%	30.9%
Male, %	55.4%	51.9%	54.7%
White, %	87.9%	85.8%	78.1%
Payor, %			
Medicare	39.4%	43.7%	40.1%
Medicaid	17.5%	16.5%	21.3%
Commercial	26.1%	29.0%	24.6%
Self-pay	12.8%	6.1%	9.0%
Charlson comorbidity score	1.5±2.0	2.3±2.7	2.0±2.5
CCI = 0	47.0%	36.5%	38.7%
CCI = 1	19.7%	17.5%	20.9%
CCI = 2	11.3%	11.4%	11.4%
CCI ≥ 3	21.9%	34.6%	29.0%
Most frequent comorbidities, %			
Diabetes w/o complication	28.3%	34.5%	31.7%
Diabetes w complication	12.3%	15.3%	11.4%
Chronic pulmonary disease	20.2%	25.9%	24.3%
Renal disease	12.3%	20.5%	16.1%
Peripheral vascular disease	9.9%	15.6%	12.3%
Congestive heart failure	10.6%	16.7%	14.9%

	Oritavancin (N=406)	Daptomycin (N=8,941)	Vancomycin (N=154,384)
Infection severity, %			
Life-threatening	3.0%	8.8%	5.8%
Systemic symptoms w/o life-threatening condition	6.7%	13.0%	13.2%
None of systemic symptoms	90.4%	78.2%	81.0%
Region, %			
South	77.6%	50.0%	50.0%
Midwest	7.1%	24.9%	18.9%
West	11.3%	14.0%	17.2%
Northeast	3.9%	11.1%	13.9%
Bed size, %			
0 - 99	8.9%	6.6%	7.9%
100-299	56.4%	36.6%	37.5%
300-499	9.4%	34.0%	28.4%
500+	25.4%	22.8%	26.2%
Teaching status, %	23.2%	36.9%	35.3%
Urban, %	91.4%	87.2%	85.7%

TABLE 2. DEMOGRAPHIC AND INFECTION SEVERITY BY INPATIENT AND OUTPATIENT

	Inpatients			Outpatients		
	Oritavancin (N=127)	Daptomycin (N=6,110)	Vancomycin (N=118,227)	Oritavancin (N=279)	Daptomycin (N=2,831)	Vancomycin (N=36,157)
Age (years)	52.7±17.7	56.1±16.8	56.5±18.0	54.9±17.1	54.0±17.0	48.9±17.5
Male, %	58.3%	49.7%	53.7%	54.1%	56.6%	57.7%
White, %	84.3%	84.2%	77.9%	89.6%	89.3%	78.8%
Charlson Comorbidity score	1.9±2.3	2.6±2.8	2.2±2.6	1.3±1.9	1.5±2.4	1.1±1.9
CCI = 0	37.0%	27.6%	32.9%	51.6%	55.6%	57.6%
CCI = 1	21.3%	19.2%	21.2%	19.0%	13.6%	19.8%
CCI = 2	15.7%	13.2%	12.5%	9.3%	7.6%	7.8%
CCI ≥ 3	26.0%	39.9%	33.4%	20.1%	23.2%	14.8%
Most frequent comorbidities, %						
Diabetes w/o complication	27.6%	39.0%	34.4%	28.7%	24.9%	23.1%
Diabetes w complication	13.4%	16.7%	13.1%	11.8%	12.3%	5.9%
Chronic pulmonary disease	27.6%	29.5%	26.8%	16.8%	18.0%	15.9%
Renal disease	15.0%	25.1%	18.7%	11.1%	10.8%	7.5%
Peripheral vascular disease	11.0%	16.9%	14.2%	9.3%	12.8%	6.0%
Congestive heart failure	18.1%	19.7%	17.3%	7.2%	10.2%	7.0%
Infection severity, %						
Life-threatening	7.1%	12.4%	7.1%	1.1%	1.1%	1.3%
Systemic symptoms w/o life-threatening condition	11.0%	17.3%	15.0%	4.7%	3.6%	7.7%
None of systemic symptoms	81.9%	70.3%	77.9%	94.3%	95.3%	91.0%

Potential impact of oritavancin

- We estimated the expected admission rate and LOS if 163,325 vancomycin and daptomycin patients were treated with single-dose oritavancin. The literature5, 6 indicate that comorbidities (CCI score) and infection severity are two of the most significant factors for physicians to determine the treatment pathway and LOS in a hospitalized patient. Within each grade of CCI score and infection severity, we replaced the admission rates of vancomycin and daptomycin patients with the admission rate of oritavancin patients, and then estimated the weighted, overall admission rate based on proportions of patient distribution within each grade. The expected LOS was calculated in the same fashion.
- The admission rate would be dropped from 76.1% to an expected 35.1% if vancomycin and daptomycin patients were treated with oritavancin.
- If hospitalized, the LOS would be dropped from 4.88 days/per admission to expected 4.35 days if treated with oritavancin.
- In 163,000 SSTI patients, adopting oritavancin could save hospitals ~356K bed days from hospital avoidance and shortening LOS.

TABLE 3: OUTCOMES AND RESOURCE UTILIZATION

	Oritavancin (N=406)	Daptomycin (N=8,941)	Vancomycin (N=154,384)
Emergency room visit, %	53.0%	59.7%	77.9%
Hospitalization rate, %	31.3%	68.3%	76.6%
30-day* all-cause admission/re-admission, %	8.6%	15.3%	12.2%
Patients treated as inpatients:			
LOS (days)	4.31±3.09	7.24±9.46	4.76±4.60
30-day* all-cause readmission, %	14.2%	17.3%	13.1%
Patients treated as outpatients:			
30-day* all-cause admission, %	6.1%	11.0%	9.3%

*30-day admission/readmission was defined as the hospitalization within the same month or next month after initial infection, due to lack of admission/discharge date per HIPPA requirement.

FIGURE 1: ADMISSION RATE BY TREATMENT STRATEGY AND CCI SCORE/INFECTION SEVERITY

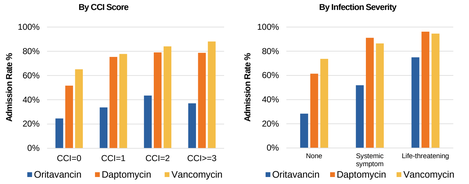
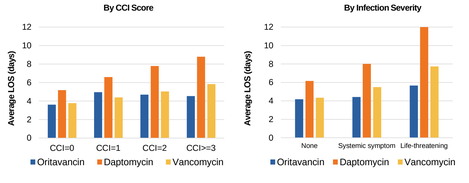


FIGURE 2: AVERAGE LOS BY TREATMENT STRATEGY AND CCI SCORE/INFECTION SEVERITY



Limitations

- Inherent in most secondary database analyses, we have assumed that hospitals have coded ICD-9 (or ICD-10) accurately and consistently; there was no source verification across with the original medical charts.
- The available data were derived from administrative records rather than a prospectively defined and standardized data collection.
- Full clinical details, such as clinical and microbiological cure, are not available in the Premier database.
- Oral antibiotics use outside of hospital was not available for Premier database.
- Patient adherence to daily IV antibiotics is unknown.
- Despite those limitations, the data were derived from a broad sample of both hospitals and patients and are representative of most current real world use of oritavancin and treatment patterns for skin infection patients.

CONCLUSION

- This analysis found that, when used in the inpatient setting, oritavancin was most frequently administered at time of discharge, indicating that oritavancin may be used as part of an early discharge strategy.
- In the outpatient setting, more oritavancin patients had chronic renal disease compared to vancomycin outpatients. This may be due to oritavancin not requiring dosing adjustments for patients with renal impairment, while vancomycin requires adjustments and monitoring due to risk of nephrotoxicity.
- This analysis finds that use of oritavancin avoided hospitalization and shortened length of stay for appropriate skin infection patients in US hospitals compared to the most frequently used IV antibiotics vancomycin and newer, less-frequent-dosing daptomycin. As skin infections represent 2% of all US hospital admissions, increased use of oritavancin may represent an opportunity to recover several hundred thousand bed days for use with other patients.

REFERENCES

1. Healthcare Cost and Utilization Project (HCUP). Overview of the National Emergency Department Sample. Agency for Healthcare Research and Quality, Rockville, MD. January 2016. Available at: https://www.hcup-us.ahrq.gov/nedsoverview.jsp. Accessed April 9, 2016.
2. Sulham K, LaPensee K, Fan W, Lodise TP. Severity and costs of acute bacterial skin and skin structure infections by treatment setting: an application of the Eron classification to a real-world database. Poster presented at: ISPOR 19th Annual International Meeting; May 31-June 4, 2014; Montreal, QC, Canada. Available at: http://www.ispor.org/research_pdfs/46pdffiles/PIN99.pdf. Accessed April 9, 2016.
3. Hersh AL, Chambers HF, Maselli JH, Gonzales R. National trends in ambulatory visits and antibiotic prescribing for skin and soft-tissue infections. Arch Intern Med. 2008;168(14):1585-91.
4. Kaye KS, Patel DA, Stephens JM, et al. Rising United States Hospital Admissions for Acute Bacterial Skin and Skin Structure Infections: recent trends and economic impact. Plos One 2015.
5. Lodise TP, Fan W, Sulham KA. Hospital admission patterns in adult patients with skin and soft tissue infections: Identification of potentially avoidable hospital admissions through a retrospective database analysis. Hosp Pract. 2015;43(3):137-43
6. Eron LJ et al, Managing skin and soft tissue infections: expert panel recommendations on key decision points. Journal of Antimicrobial Chemotherapy 2003;52:i3-i17.
7. LaPensee K, Fan W. Economic Burden of hospitalization with Antibiotic Treatment for ABSSSI in the US: An analysis of the Premier Hospital Database. ISPOR 2012 poster.