Evaluation of Oritavancin Use at a Community Hospital

Hospital Pharmacy
2018, Vol. 53(4) 272–276
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DOI: 10.1177/0018578717746415
journals.sagepub.com/home/hpx

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Abstract

Background: Oritavancin is a lipoglycopeptide antibiotic indicated for the treatment of acute bacterial skin and soft tissue infections. The prolonged half-life of this agent allows for a course of therapy to be completed with a single dose. Oritavancin was added to our formulary as an option for treatment of acute bacterial skin and soft tissue infection to reduce admission and length of stay. **Objective:** The purpose of this study was to determine whether oritavancin is used appropriately at our hospital and to evaluate the impact to the institution. **Methods:** A retrospective and concurrent chart review was performed on all patients who had received oritavancin within our health system between June 2015 and December 2016. The primary endpoint was to determine the appropriateness of oritavancin use. Secondary endpoints include documenting readmission rates for patients prescribed oritavancin and assessing potential financial benefits to the institution. **Results:** In the 67 patients identified, 51 (76%) patients received oritavancin for an appropriate indication. Orders from infectious disease physicians constituted 81% of inappropriate cases of oritavancin use. No patients who received oritavancin required readmission within 14 days of therapy. The estimated potential financial benefit to our institution when using oritavancin to prevent hospital admissions was \$653,451. **Conclusions:** The majority of oritavancin use at our institution is appropriate according to indication. Oritavancin offers an outpatient option for the treatment of acute bacterial skin and soft tissue infections with the potential to decrease hospital cost by reducing admissions and length of stay.

Keywords

anti-infectives, cost effectiveness, drug/medical use evaluation, infectious diseases

Background and Objective

The treatment of acute bacterial skin and soft tissue infections (ABSSTIs) remains a significant economic burden to patients and hospitals across the United States. ABSSTIs contribute to the rapidly expanding volume of emergency department (ED) visits and are attributed to roughly 10% of all US hospital admissions.¹ The Infectious Diseases Society of America (IDSA) recommends that these infections be treated with 5 to 14 days of antibiotics,² often requiring a multiple day admission with the associated costs of room, medications, laboratory tests, intravenous lines, and so on.

In August 2014, the US Food and Drug Administration (FDA) approved the lipoglycopeptide antibiotic oritavancin (Orbactiv; The Medicines Company, Parsippany, New Jersey) for the treatment of adult patients with ABSSTIs. Oritavancin is indicated for the treatment of infections caused by certain gram-positive organisms,³ including *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA). A course of therapy for oritavancin consists of one 1200-mg intravenous dose, making it the first single-dose treatment option for ABSSTIs approved by the FDA. Dosing for oritavancin

does not require adjustment for patient weight, age, renal impairment, or hepatic impairment.³

Because a course of therapy can be completed with a 1-time infusion, it has been postulated that oritavancin may be used in a cost avoidance strategy to shorten length of stay or even eliminate the need for a hospital admission to treat an ABSSTI. Data to support the use of oritavancin as an alternative to inpatient treatment are provided by the SOLO I and SOLO II trials, two phase III, randomized, multicenter, international, double-blind studies which compared the efficacy and safety of single-dose oritavancin with 7 to 10 days of intravenous vancomycin in adults with ABSSTIs. For the efficacy assessments of cessation of spread/reduction in size of baseline lesion, absence of fever, need for rescue antibiotics, and investigator-assessed clinical cure 7 to 14 days after the end of treatment, the results of these trials showed no

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difference between the oritavancin and vancomycin groups.^{4,5} The overall frequency of adverse events was also similar between treatment groups. The confirmation of noninferiority of oritavancin to vancomycin by these studies suggests that single-dose oritavancin provides an alternative to multi-dose antibiotic therapy for treatment of ABSSTIs.

Based on this data and potential for cost savings, oritavancin was added to the formulary of our large community hospital in June 2015 as an option to reduce admissions due to ABSSTIs. The objective of this analysis was to evaluate the use of oritavancin within our hospital since its addition to formulary, and to determine the financial impact of oritavancin use to the institution.

Methods

In this study approved by our hospital Institutional Review Board, a retrospective chart review was used to obtain data for all patients who had received oritavancin through our health system from June 2015 to October 2016. Data were collected from the hospital electronic medical records (EMRs), as well as from clinical notes documented in our pharmacy surveillance software. A drug utilization report was generated from the EMR and used to identify all patients who had received oritavancin during the specified time period. Based on this report, 67 patients were identified and included in the study. The following data points were collected for each patient: age, gender, prior antibiotic use, indication for oritavancin, prescriber, and admission dates.

The primary outcome of the study was to determine the appropriateness of oritavancin use by indication, using institution-specific restricted antimicrobial criteria for use for oritavancin. Based on these criteria for use and FDA-approved indication, oritavancin use was considered appropriate if used in the treatment of patients with ABSSTIs, including cellulitis, cutaneous abscess, and wound infections. Use in patients for the treatment of non-FDA-approved indications, such as osteomyelitis and bacteremia, was considered inappropriate for the purpose of this study.

Secondary outcomes included the number of readmissions in patients treated with oritavancin and the financial impact of oritavancin use to our institution. A readmission was documented for any patient who returned to our health system within 14 days of oritavancin administration. Readmission data were only collected for patients who presented back with complaints of the same infectious process.

Potential financial benefit was calculated by comparing the cost of hospitalization for inpatient treatment of an ABSSTI with the cost of a dose of oritavancin. The cost of inpatient treatment was calculated by multiplying the duration of hospitalization (in days) by the cost-per-day of a hospital bed. Potential financial benefit was assessed using 340B pricing for drug acquisition cost and a national average for cost-per-day for treatment of ABSSTIs. An institution-specific length of stay (6.62 days) was calculated using

Table 1. Indications for Oritavancin Use.

Indication	No. of patients (%) ^a
Cellulitis	37 (49.3)
Abscess	8 (10.6)
Cardiac device infection ^b	7 (9.3)
Diabetic foot infection	3 (4.0)
Miscellaneous SSTI ^c	4 (6.6)
Septic arthritis	5 (7.5)
Osteomyelitis	8 (10.6)
Bacteremia	3 (4.0)

Note. SSTI = skin and soft tissue infection.

^aPatients with 2 indications were included in both categories.

^bRedness and swelling around the surgical site of a recently implanted cardiac device.

^cIncludes knee infection, leg wound (unspecified), folliculitis, ulcer (unspecified).

admissions with diagnosis codes for skin and soft tissue infections over the last year.

Results

A total of 67 patients were identified and included in this study. Of these patients, 41 (61%) were male and 26 (39%) were female. Patient age ranged from 19 to 90 years old, with a mean age of 52.3 years old for this population. The majority of patients (90%) received oritavancin as outpatients through our outpatient infusion center and in the ED; a smaller portion of the patients (10%) were given the drug in the inpatient setting, just prior to discharge. A total of 41 patients (61%) had previous antibiotic use prior to receiving oritavancin therapy; this includes both intravenous and oral medications, and only those intended to treat the infection for which oritavancin was eventually prescribed.

A list of the indications for which oritavancin was prescribed in this population is reported in Table 1. In this population, 51 (76%) patients received oritavancin for an indication which was considered appropriate. In contrast, 16 (24%) received oritavancin for an inappropriate indication. The most common appropriate indication for which oritavancin was used was cellulitis (49.3%), whereas the most common inappropriate indication was osteomyelitis (10.6%).

Prescribing patterns by department are as follows: 6 (9%) of orders prescribed by hospitalists, 17 (25%) prescribed by ED physicians, 8 (12%) prescribed by cardiologists, and 36 (54%) prescribed by infectious disease physicians. Infectious disease physicians include both our hospital-employed infectious disease group and a private infectious disease group who see patients at our institution. Prescribing patterns of inappropriate use, described by department, are shown in Figure 1.

There were no patients who had to be readmitted to our facilities within 14 days of oritavancin therapy. A total of 8 patients (12%) presented back to the ED with complaints of

Figure 1. Oritavancin Prescribing Patterns.
Note. ED = emergency department; Hospital ID = hospital-based infectious disease group; Private ID = private infectious disease group.

Table 2. Potential Financial Benefit.

Average length of stay for cellulitis	6.62 days
Hospital bed cost-per-day	\$1,999 ^a
Cost per dose of oritavancin	\$3,480 ^b
Amount saved per patient	\$9,753
Number of patients per year	67
Annual savings	\$653,451

Note. ABSSTIs = acute bacterial skin and soft tissue infections.
^aNational average for ABSSTIs.⁶
^bAverage wholesale price (AWP) cost of Orbactiv 400 mg vial × 3.

the same infection within 14 days of oritavancin therapy; however, none of these patients were admitted. There was no correlation between patients who presented back to the ED and inappropriate use of oritavancin.

Table 2 illustrates the estimated financial benefit to the hospital if oritavancin is used as an alternative to admitting patients for the treatment of a cellulitis. Assuming a 6.62 day hospital stay is prevented, the estimated amount saved per patient is \$9,753. If applied to the current sample size, appropriate use of oritavancin to prevent admissions for ABSSTIs has the potential to save our hospital an estimated \$653,451 annually.

Discussion

Previous studies⁷ have suggested that, in comparison with standard therapy for ABSSTIs, treatment with oritavancin has the potential to reduce complications associated with multiple intravenous administrations, improve adherence, improve quality of life, and to reduce the utilization of health care resources. However, to achieve these benefits, it is necessary

to use oritavancin in a way outlined by the evidence, and therefore for the approved indications. Patients considered eligible for oritavancin therapy include those who would require hospitalization only for treatment of an ABSSTI which is suspected or confirmed to be unresponsive to alternative oral antibiotic therapies. Patients with concurrent illness who require hospitalization regardless the treatment option chosen for ABSSTIs should not be considered eligible for oritavancin therapy.

The results of the current study show that the majority of oritavancin use at our hospital was appropriate according to indication, with 76% of patients treated for cellulitis, cutaneous abscess, wound infection, or miscellaneous skin infections. The remainder of oritavancin use (26%) was in patients with bacteremia, septic arthritis, osteomyelitis, or other infections for which the drug has not been studied in clinical trials, and was therefore considered inappropriate. Appropriateness of oritavancin use during this study was determined on a case-by-case basis, by reviewing physician progress notes, other antibiotic orders, documented International Classification of Diseases (ICD) code, and clinical pharmacist documentation. Determination of appropriateness was not made based upon a single factor, but the pool of available data for each patient.

A subanalysis was performed on patients with oritavancin orders which were considered inappropriate to determine which providers and which departments within the hospital most frequently prescribed oritavancin inappropriately (Figure 1). The results of this analysis show that an overwhelming majority of inappropriate oritavancin orders came from infectious disease physicians. In this analysis, the 2 infectious disease groups which practice within our institution were differentiated; these groups are the hospital-based infectious disease physician group and a local (private) infectious disease group which serves patients in our region.

Appropriate

- Acute infection requiring presentation to emergency department, urgent care, or hospital
- Infection severe enough to require IV antibiotic therapy, in patients who are otherwise candidates for outpatient treatment
- Failure or intolerance to oral antibiotics
- No major comorbidities which require acute management and hospitalization (including sepsis)
- Situations in which compliance or access to outpatient parenteral antibiotic therapy may be challenging
- Treatment of a disease state for which oritavancin has FDA approval (skin and soft tissue infections)

Inappropriate

- Inpatient treatment for situations in which other anti-infectives (i.e. vancomycin) are appropriate
- Treatment of a disease state for which oritavancin does not have an FDA approval (including but not limited to: MRSA pneumonia, bacteremia, septic arthritis, osteomyelitis, endocarditis, MRSA infection of CNS)
- Contraindications or drug interactions exist which would interfere with either therapy

Figure 2. Sample Oritavancin Use Criteria.

Further analysis of the data revealed that 75% (13 patients) of the total inappropriate cases were attributed to a single provider from the private infectious disease group. Of note, oritavancin orders prescribed by cardiologist were all appropriate, as the indication was for treatment of cellulitis around pacemaker insertion sites.

Education to providers concerning appropriate prescribing habits and compliance with criteria for use of oritavancin was achieved by both one-on-one discussions of specific cases with the provider from the private infectious disease group, as well as educational in-services to various hospital committees highlighting the results of this study and our oritavancin criteria for use. Based on our institutional criteria for use and the results of this study, a sample of use criteria are listed in Figure 2 which may be used for provider education and the development of antibiotic policies at other institutions.

One data point included in the baseline characteristics was the number of patients with prior antibiotic use. Prior antibiotic use was recorded for any patient who had received antibiotic therapy with the intent to treat the same infection for which oritavancin was prescribed. Patients receiving empiric broad-spectrum therapy or antibiotics intended to treat another infection were not included in this data point. The majority of prior antibiotic use was in treatment failure of patients treated with outpatient oral antibiotics, including clindamycin, sulfamethoxazole-trimethoprim, cephalexin, amoxicillin-clavulanate, and doxycycline.

A secondary outcome in this study was to determine the number of patients readmitted to our health system facilities within 14 days of oritavancin therapy. The 14-day window was chosen based on the time point for posttherapy clinical evaluation (PTE) used in the SOLO I and SOLO II trials.^{4,5} While no patients required readmission as inpatients after receiving oritavancin, a total of 8 patients returned to the ED with complaints of worsening or persistence of the infection. Upon evaluation by ED providers, none of these patients were found to have symptoms severe enough to require hospitalization. The majority of these patients were prescribed alternative oral therapy (including clindamycin, amoxicillin-clavulanate, and doxycycline) and allowed to return home. Other patients were instructed to use warm compresses and acetaminophen as needed for

pain, and also allowed to return home. While the persistence of symptoms may suggest treatment failure, these patients returned to the ED within 24 to 72 hours after their initial discharge and were not found to have symptoms severe enough to indicate treatment failure when evaluated by emergency medicine providers. The cost of additional therapy and visits to the ED was not addressed in this study, but may be include as part of a more robust financial analysis. It is also important to note that due to the limitations of the data collection method, only patients who returned to a facility within our health system could be documented. The true number of patients who required subsequent care may be higher when accounting for patients treated at another health care system, a primary care provider office, or an urgent care clinic within 14 days of receiving oritavancin. Based on this information, our study failed to show an association between indication and readmission for patients treated with oritavancin.

The final outcome addressed in this study was the potential financial benefit of oritavancin use to the institution. In this analysis, annual savings were estimated according to the following assumptions: Oritavancin is used for an appropriate indication and administered to a patient before the patient is ever required to be admitted; the average length of stay for treatment of ABSSTIs (and therefore the potential number of inpatient days saved) is 6.62 days; the annual number of patients eligible for admission-sparing therapy with oritavancin is similar to the sample size ($n = 67$) of patients included in this study. Because the goal of adding oritavancin to hospital formulary was to reduce ABSSTI hospital admissions, patients who failed therapy with oritavancin and required a subsequent admission would constitute a negative financial impact to the institution. As there were no subjects who required a full readmission after oritavancin therapy in this study, readmission costs were not included as part of the financial analysis.

Using a national average⁶ ABSSTI cost-per-day of \$1,999 and AWP pricing for cost of drug, the estimated annual savings was greater than \$650,000. This estimated annual savings may be applied to other institutions by substituting institution-specific figures for average length of stay, cost-per-day, drug acquisition cost, and anticipated number of eligible patients.

Previous authors⁸ have used more in-depth financial models, taking into account the cost of intravenous lines, lab tests and drug monitoring, and cost of treating adverse reactions. The in-depth analysis also differentiated inpatient and outpatient costs, considering costs across observation, admission, and discharge of the patient. As a future direction to our study, a more robust financial analysis would solidify the benefits of oritavancin as a cost-sparing option to our institution.

The length of stay used in this analysis was initially based on the average length of stay for treatment of cellulitis, 14 days, cited in the Infectious Disease Society of America Guidelines on Skin and Soft Tissue Infections.² However, a 14-day average length of stay for cellulitis, while endorsed by the IDSA SSTI guidelines, may overestimate the true number of days required to treat ABSSTI patients at our hospital and other institutions. A recent study looking at trends and economic impact of ABSSTIs in the United States found that the mean hospital length of stay was between 5.4 and 5.0 days for adult inpatients with a primary diagnosis of ABSSTIs.⁶ The institution-specific average length of stay (6.62 days) used in this analysis may therefore provide a more accurate figure to the national average than the figure cited in the IDSA guidelines.

One limitation to this study was the use of a national average for hospitalization cost-per-day instead of an institution-specific cost. The cost of hospitalization is multifactorial and would have been prohibitively complex to calculate for the purposes of this study; the cost of other medications, lab tests, and medication administration costs (including intravenous lines) would need to be taken into account, in addition to the cost of a hospital room and other factors. Similarly, the AWP cost of drug used in this analysis does not take into account reimbursement through the manufacturer's patient assistance program, nor any group purchasing organization (GPO) or 340B discounts, and may not represent true acquisition cost for our institution.

As a future direction to this study, a more robust financial impact analysis could be performed which would take into account the number of days a patient had been admitted before receiving oritavancin. The number of days a patient had been admitted would be subtracted from the average number of days for ABSSTI hospitalization, to provide a more accurate representation of how many days of hospitalization were saved for each patient using oritavancin therapy. A more robust financial analysis would also include the cost of ED visit for patients with complaints related to the disease state for which oritavancin was prescribed, as well as any potential costs (eg, additional antibiotic therapies prescribed) associated with these ED visits.

Conclusion

The results of our study showed that the majority of oritavancin use within a community hospital was appropriate according to indication, and was most commonly ordered by infectious disease physicians. If used appropriately as an outpatient alternative for the treatment of ABSSTIs, oritavancin could save our institution over \$650,000 annually by preventing hospital admissions. While the current financial analysis may lack certain institution-specific figures, oritavancin is still expected to have potential for significant financial benefit to our hospital.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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