P0283

Potential Cost Savings Opportunities with Targeted Use of Iclaprim (ICL) Compared to Vancomycin (VAN) among Hospitalized Patients with Acute Bacterial Skin and Skin Structure Infections Due to Potential Avoidance of VAN-Associated Acute Kidney Injury V-A AKI

N. Patel[1], D.B. Huang[2], T.P. Lodise[1]

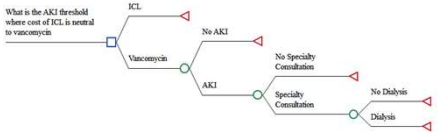
[1]Albany College of Pharmacy & Health Sciences, Department of Pharmacy Practice, Albany, NY, USA; [2]Motif BioSciences, New York, NY, USA

Correspondence:
Thomas Lodise, Pharm.D., Ph.D.
Professor, Department of Pharmacy Practice
Albany College of Pharmacy & Health Sciences
106 New Scotland Avenue
Albany, NY 12208
USA

ABSTRACT (REVISED)

Background: Vancomycin (VAN) is the most prescribed antibiotic for hospitalized adults with skin and skin structure infections (SSSIs). VAN is associated with V-A AKI. Iclaprim (ICL) is an antibiotic under development for treatment of patients with acute bacterial SSSIs (ABSSSI). In two phase 3 ABSSSI studies, ICL was not associated with AKI. This economic model sought to determine the potential cost savings opportunities with ICL compared to VAN among hospitalized patients with ABSSSI due to potential avoidance of V-A AKI.

Materials/Methods: A cost-minimization model from the hospital perspective was developed to estimate the overall incremental cost impact of replacing empiric VAN with ICL among hospitalized adult SSSI patients. The structural model (figure) included: VAN acquisition ($42.80/day x 7 days (RedBook)); VAN assay ($18.58/assay x 5 in the absence of VA-AKI and 8 in the presence of V-A AKI); incidence of V-AAKI: 9.2% (V-A AKI rate observed in hospitalized patients at the Veterans Affairs Medical Center with SSSI); excess length of stay at hospital if V-A AKI occurred ($1,585.69/day x 5 days); frequency of specialty physician consults after occurrence of V-A AKI: 25%; cost of specialty physician consults ($485 per consult x 5 consults); probability of acute dialysis due to V-A AKI: 15%; and cost of acute dialysis ($1590.82 x 1 session). ICL treatment duration was 7 days and ICL acquisition cost was varied to determine the upper end of the daily ICL price that still conferred cost savings with ICL relative to VAN. Duration of hospitalization for ICL was assumed to be the same as patients with no V-A AKI.



Results: Based on the overall rate (9.2%) of V-A AKI among SSSI patients, the neutral acquisition price threshold for ICL versus VAN was $1210.26/regimen ($172.89/day). Across various subpopulations where V-A AKI risk ranged between 9.2% to 16.7%, the upper end of the daily ICL acquisition cost that still conferred cost savings varied between $150 – 300/day.

Conclusion: Iclaprim has the potential to reduce the economic burden of ABSSSIs in hospitalized patients at risk for V-A AKI when ICL acquisition is between $150-300/day.

BACKGROUND

- While vancomycin is considered the first line treatment option and most frequently used antibiotic for adult hospitalized patients with acute bacterial skin and skin structure infections (ABSSSIs), acute kidney injury (AKI) is a major concern with its use.
- Risk of vancomycin-associated AKI varies across patient populations and high risk groups include patients with certain comorbidities such as diminished renal function, obesity and higher disease severity.
- Patients who experience vancomycin-associated AKI have an increased risk of death, have extended hospital length of stay (LOS), and often require additional levels of care such as a specialty physician consultations and acute dialysis sessions.
- Given the increased mortality and costs associated with the management of patients who experience vancomycin-associated AKI, alternative treatments, particularly among populations at an elevated risk for vancomycin-associated AKI should be considered.
- Iclaprim is a diaminopyrimidine antibiotic that is under development for treatment of patients with ABSSSIs
  - Rapid bactericidal activity *in vitro* against Gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA).
  - Does not require dose adjustments for patients renal impairment and does not appear to cause AKI

OBJECTIVES

- The purpose of this study was to examine the economic impact of shifting from use of intravenous vancomycin to an agent with a low potential for AKI, such as iclaprim, among hospitalized patients with ABSSSI.
  - Developed conceptual healthcare decision models for hospitals to estimate the daily drug cost thresholds where it would be prudent to consider an agent like iclaprim over vancomycin for the treatment of adult hospitalized patients with ABSSSIs by averting the occurrence of vancomycin-associated AKI.
  - Quantified the daily iclaprim cost associated with a potential savings due to avoidance of vancomycin-associated AKI in various ABSSSI subpopulations.

METHODS

Model Structure & Population

- Used a deterministic framework from the US hospital perspective to develop the decision analytic model that replaced use of empiric intravenous vancomycin with iclaprim for the treatment of inpatients with ABSSSIs. (Figure, abstract)
- The population was hospitalized, adult patients with ABSSSIs and patients were allocated to one of two empiric treatment states: vancomycin or iclaprim. For vancomycin recipients, a proportion of patients were expected to develop vancomycin-associated AKI.

Model Inputs

- The full list of items and associated excess costs considered are included in Table 1.
- Treatment duration for both groups was assumed to be 7 days. (Huang DB et al. Clin Infect Dis. 2017)
- Emergency department, hospital and all process of care costs were assumed to be equal during the initial 7-day treatment period.

Vancomycin-specific inputs

- Vancomycin costs during the initial 7-day treatment period included drug (2 grams per day) and vancomycin serum concentration monitoring
  - Wholesale Acquisition Cost (WAC) of vancomycin powder for solution (Hospira) from the RedBook was used for the price of vancomycin.
  - Vancomycin assay cost ($18.58/assay) associated with therapeutic drug monitoring (TDM) were obtained from the Medicare Laboratory Fee Schedule.
    - Assumed patients had five concentrations collected over the initial 7-day treatment period.
- Given the paucity of real-world data describing the incidence of vancomycin-associated AKI and subsequent healthcare resource utilization among ABSSSI patients, a retrospective cohort study was conducted among hospitalized patients with skin and skin structure infections (SSSIs) in the Upstate New York Veterans' Healthcare Administration (ECCMID Poster #E0283).
- The following outcomes were extracted: (1) occurrence of vancomycin-associated AKI, defined as a 0.5 mg/dL increase in serum creatinine or 50% decline in calculated creatinine clearance (CLCR, Cockroft Gault method) after initiation of vancomycin, (2) hospital LOS among patients who experienced vancomycin-associated AKI versus those that did not, (3) receipt of specialty physician consultation services (i.e. nephrology or infectious diseases consult) after occurrence of vancomycin-associated AKI, and (4) receipt of acute dialysis after occurrence of vancomycin-associated AKI.
  - Outcomes were also extracted from sub-populations expected to have an elevated risk of vancomycin-associated AKI. The specific sub-populations included patients with diabetes, obesity (body mass index, BMI ≥ 30), impaired renal function (CLCR 30 – 50 ml/min) and previous episode of vancomycin-associated AKI.

Iclaprim-specific inputs

- All iclaprim patients were assumed to have received 7 days of treatment as an inpatient and discharged home with presumed resolution of the ABSSSI episode.
- In the initial model, the cost of iclaprim varied from $150 to $450/day to estimate the upper end of daily iclaprim acquisition cost that still conferred cost savings relative to vancomycin treatment.

Model Outputs

- The outputs of the model included mean weighted excess per-patient total and individual component costs of vancomycin at all levels of the structural model (Figure 1).
- Overall per patient excess cost differences between vancomycin and iclaprim were calculated at different daily iclaprim costs.

Sensitivity Analyses

- Three sets of sensitivity analyses were performed to determine the impact of varying model inputs on the upper end of daily iclaprim acquisition cost that still conferred cost savings relative to vancomycin treatment.
  - Daily hospital cost were varied ($2000 to $3000/day in $500/day increments) given the variability in costs across US hospitals.
  - Daily cost of iclaprim were varied from $150/day to $400/day (in $50/day increments) during the initial 7 treatment period to quantify the vancomycin-associated AKI threshold where iclaprim would result in savings.
  - Frequency of vancomycin-associated AKI was varied based on the rates observed in sub-populations of Veterans Affairs patients (diabetes, obesity, impaired renal function and history of vancomycin-associated AKI.
- All analyses were performed in SPSS (v24, Armonk, NY) and TreeAge Pro (2018, Williamstown, MA).

RESULTS

Table 1: Budget Impact Model Costs Associated With Inpatient Vancomcyin Versus Iclaprim

Item	Cost
Vancomycin Costs	
Vancomycin intravenous therapy (2g/day) was assumed to be $42.80/day[1] x 7 day course of therapy	$299.60
Vancomycin monitoring was assumed to be $18.58/assay[2] x 5 assays during course of treatment	$92.90[1]
Each hospital day after V-AKI was assumed to cost 1585.69 dollars[3] x 5 days (median excess LOS observed)	$7,928.45
The cost of nephrology/infectious diseases physician consult was assumed to be $485/day[4] and carried forward for five of the excess hospitalization days for patients experiencing V-AKI	$2,425.00
The cost of additional vancomycin serum concentration was assumed to be $18.58/assay[2] x 3 assays during the excess hospitalization days for patients experiencing V-AKI	$55.74
The cost of one session of high-flux acute dialysis[5] was assumed to be $1590.82/session[5]	$1,590.82
NOT INCLUDED: Pharmacist time for processing medication orders or analyzing vancomycin serum concentrations, subsequent outpatient follow-up costs, patient satisfaction with treatment, patient quality of life, patient productivity costs, risks and complications associated with IV treatment[3]	N/A
Iclaprim Costs	
Cost of iclaprim varied in models from $150/day to $400/day, in $50/day increments	Varied
NOT INCLUDED: Pharmacist time for processing medication order/reviewing drug-drug interactions, subsequent outpatient follow-up costs, patient satisfaction with treatment, patient quality of life, patient productivity costs, risks and complications associated with intravenous treatment, infectious diseases specialty physician to review/approve restricted antimicrobials, costs of ECG monitoring.	N/A
Both Vancomycin and Iclaprim Costs	
ED and inpatient treatment costs assumed equal for each agent until occurrence of V-AKI	Null
Treatment duration was assumed to be 7 days for each drug	Null
Hospital and process of care costs during initial 7 days were assumed to be equal for each agent	Null

Legend:ED – emergency department, ECG – electrocardiogram, V-AKI – vancomycin-associated acute kidney injury.
[1]RedBook. Truven Health Analytics. Micromedex Solutions. WAC cost of Hospira Vancomycin 10 G powder for solution (NDC: 00409-6510-01). Effective date May 2016.
[2]Clinical Laboratory Fee Schedule. Centers for Medicare and Medicaid Services. 2016. Available at: https://www.cms.gov/apps/ama/license.asp?file=/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Downloads/17CLAB.zip
[3]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 (1995). 2015;43(3):137-43. Median weight cost of hospital day for patients with skin infections. Data inflated to current costs using healthcare CPI.
[4]Obtained from Healthcare Bluebook. CAREOperative LLC. Nashville, TN. 2018
[5]Kshirsagar A, Hogan SJ, Mandelkehr L, Falk RJ. Length of Stay and Costs for Hospitalized Hemodialysis Patients: Nephrologists versus Internists. J Am Soc Nephrol 11: 1526–1533, 2000. Data inflated to current costs using healthcare CPI.

Table 2: Model Inputs For Frequency Of Vancomycin-Associated Acute Kidney Injury And Excess Healthcare Utilization Among Veterans Affairs Patients With Acute Bacterial Skin And Skin Structure Infections

Population	Point Estimate
Overall frequency vancomycin-associated AKI	9.2%
• Patients with diabetes mellitus	9.0%
• Patients with diminished renal function (CLCR 30 – 50 ml/min)	11.5%
• Patients with body mass index ≥ 30	9.3%
• Patients with previous history of vancomycin-associated AKI	16.7%
Healthcare utilization	
Excess hospital length of stay among patients with vancomycin-associated AKI	5 days
Proportion of patients with vancomycin-associated AKI & requiring specialty physician consultation	25.0%
Proportion of patients with vancomycin-associated AKI, requiring specialty physician consultation & acute dialysis	15.0%

Figure 2: Threshold For Vancomycin-Associated Acute Kidney Injury Needed To Confer Cost Savings With Iclaprim

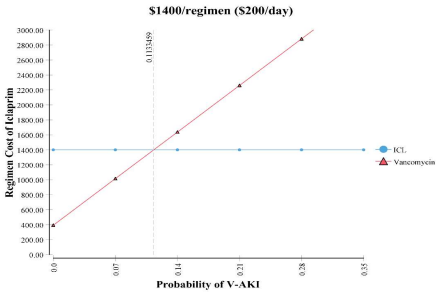


Table 3: Costs Of Vancomycin-Associated Acute Kidney Injury At Varying Daily Costs Of Hospitalization

Daily Hospitalization Cost	$1,585.69/day	$2,000/day	$2,500/day	$3,000/day
Vancomycin-associated AKI only	$8,377	$10,448	$12,948	$15,448
Vancomycin-associated AKI and specialty physician consultation	$10,802	$12,873	$15,373	$17,873
Vancomycin-associated AKI, specialty physician consultation and acute dialysis	$12,393	$14,464	$16,964	$19,464
Overall neutral iclaprim cost-threshold over vancomycin	$172.89	$200.12	$232.98	$265.83

CONCLUSIONS

- Among patients with skin and skin structure infections treated with vancomycin, the overall incidence of acute kidney injury (AKI) was 9.2%.
- Costs associated with the management of patients who experience vancomycin-associated AKI range from $8,377 to $19,464 depending on use of specialty physician consultation, receipt of acute dialysis, and daily hospital cost.
- Replacement of vancomycin with iclaprim for treatment of acute bacterial skin and skin structure infections is associated with significant cost savings for hospitals due to avoidance of vancomycin-associated AKI.
- Hospitals aspiring to minimize cost by avoidance of vancomycin-associated AKI should examine their hospital-specific rates of vancomycin-associated AKI and local costs of hospitalization to determine if replacement of vancomycin with an agent like iclaprim can confer a cost savings, especially among patients at high risk for vancomycin-associated AKI.

DISCLOSURES

Motif BioSciences sponsored work performed by IDRx Solutions LLC to derive the data presented in this manuscript. NP and TL have received investigator initiated research grant support from Motif BioSciences, Inc. DH is a paid employee of Motif BioSciences, Inc. TL has received consulting honoraria from Motif BioSciences, Inc.