

Infusion Journal

Volume 2, Issue 1 | March / April 2023

InfusionJournal.com



About the cover:

The FDA requires Risk Evaluation and Mitigation Strategies (REMS) for certain medications to prevent, monitor, and manage specific risks. These programs can impact which sites of care are considered appropriate for patient administration of IV therapies. However, rare instances—such as a national public health emergency—can offer additional insight into balancing safety and availability.

The Safety of Natalizumab Administration in the Home During the COVID-19 Pandemic for Patients with Multiple Sclerosis

Rohae Musa, PharmD

Maria Giannakos, PharmD, MBA, BCPS, BCSCP

Suzanne Kluge, B.S. Pharm, MBA, RPh, BCSCP, FNHIA

A Review of Daptomycin vs. Vancomycin for Susceptible Infections: Is One Superior for Outpatient Parenteral Antibiotic Treatment (OPAT)?

Daniel Decker PharmD, MBA, BCACP

Successful Transition from Subcutaneous Immune Globulin (SCIG) Therapy to Intravenous Immune Globulin (IVIG) Therapy in Primary Immunodeficiency: A Case Report

Amy Mulgrew, RN, CRNI, IgCN, VA-BC

Ashley McKenna, RN, IgCN

Erin Mullis, RN, IgCN

NHIF
National Home Infusion Foundation

Infusion Journal

An official publication of the
National Home Infusion Association

Editor-in-Chief

Michelle Simpson, PharmD, BCSCP, MWC

Associate Editors

Ryan Garst, PharmD, MBA, IgCP, BCSCP

Jennifer Charron, RN, MSN, MBA

Statistical and Research

Methodology Editor

Danell Haines, PhD

D.J. Haines Research Consulting

Managing Editor

Jeannie Counce

Editorial Advisory Board

David Franklin, MSA

Advanced Care Consulting Services

Mitra Z. Gavani, PharmD

Johns Hopkins Home Care Group

Chris Maksym, RPh, PharmD

University of Michigan (ret.)

Dave Grady

Big Sky IV Care

Janice Wilhelm, RN, MBA

Advanced Home Care

Drew Doyle, RPh

Soleo Health

Laila Alqadri, MD

KabaFusion

From the Editor

Michelle C. Simpson, PharmD, BCSCP, MWC
Editor-in-Chief, *Infusion Journal*

The Food and Drug Administration's (FDA) risk evaluation and mitigation strategies (REMS) drug safety program keeps drugs on the market that would otherwise be withdrawn due to safety risks. The FDA can require a REMS for certain medications with serious safety concerns. REMS are not designed to mitigate all the adverse events of a medication but focus on preventing, monitoring, or managing a specific serious risk. The requirements of a REMS can be modified or revised over time as patient safety data is collected, studied, and reported.

The natalizumab (Tysabri®) REMS was first approved in 2011, and since then, the REMS has been modified 9 times and revised 4 times.¹ It has been updated 13 times in 12 years. The REMS may have changed frequently, but it consistently restricted infusion sites of care to exclude the home as an approved site for natalizumab administration. Through the COVID-19 public health emergency (PHE) and its effect on access to care in ambulatory settings, the drug manufacturer modified the REMS to open patient access to administering natalizumab in the home for patients and providers meeting the updated REMS criteria.

The REMS modification allowing home administration offered new opportunities to study and report differences in medication safety related to the site of care. The article in this issue of *Infusion Journal* titled "The Safety of Natalizumab Administration in the Home During the COVID-19 Pandemic for Patients with Multiple Sclerosis" studied patients who received natalizumab in an infusion suite for their initial treatments and then transitioned to administration in the patient home. Previous studies reported that patients preferred home infusion, stating significantly better physical and mental health and less disruption of family and personal lifestyle patterns.² Increased access to home infusion of natalizumab gave eligible patients the option of choosing their preferred site.

The current REMS, modified as part of the PHE and allowing for the home as the site for administration, requires providers (the pharmacy and nursing service) to have additional training. Based on the results from the study presented in this issue, the modification was effective for maintaining safety in both the infusion suites and the patient's homes.

The PHE ends in May 2023, which could mean the FDA will request the REMS to return to pre-PHE strategies requiring administration only in approved infusion sites. If this happens, what will happen to the patients who received infusions at home during the PHE? Will they be considered for continued home administration? What about other patients who meet the criteria and would prefer home administration?

This is an interesting situation because of the unique events that opened access to the home for natalizumab infusions. When the drug manufacturer submits documentation to the FDA for approval of modifications to the natalizumab REMS, research from published studies like the one in this month's *Infusion Journal* may support current and future patients in expanded access. When safety outcomes are comparable, decisions for the site of care should be guided by prescribers in collaboration with the nurses and pharmacists of the home infusion pharmacy.

Infusion Journal is dedicated to publishing research on infusion therapies and welcomes submissions from authors on topics relevant to infusion therapy administered in the home, clinic, suite, or another setting.

References

1. Approved Risk Evaluation and Mitigation Strategies (REMS). Natalizumab (Tysabri) REMS History. <https://www.accessdata.fda.gov/scripts/cder/remis/index.cfm?event=IndvRemsDetails.page&REMS=63>
2. Polinski JM, Kowal MK, Gagnon M, Brennan TA, Shrank WH. Home infusion: Safe, clinically effective, patient preferred, and cost saving. *Healthc (Amst)*. 2017 Mar;5(1-2):68-80. doi: 10.1016/j.hjdsi.2016.04.004. Epub 2016 Apr 29. PMID: 28668202.

Special thanks to Baxter
for their generous
support of the 2023
Infusion Journal

Baxter

The Safety of Natalizumab Administration in the Home During the COVID-19 Pandemic for Patients with Multiple Sclerosis

Rohae Musa, PharmD
Option Care Health

Maria Giannakos
PharmD, MBA, BCPS, BCSCP
Option Care Health

Suzanne Kluge
B.S. Pharm, MBA, RPh,
BCSCP, FNHIA
Option Care Health

Contact:
rohae.musa@optioncare.com

ABSTRACT

Background

Multiple sclerosis (MS) is a progressive autoimmune inflammatory disorder causing demyelination and degeneration of the central nervous system. Natalizumab is a highly effective monoclonal antibody for the treatment of relapsing-remitting multiple sclerosis (RRMS).¹ It is usually delivered as 300 mg 1-hour intravenous infusion every 4 weeks.¹ Natalizumab is generally well tolerated, however, there are infusion-related reactions associated with the drug, and a risk of progressive multifocal leukoencephalopathy (PML). Patients were previously required to receive the infusions in an authorized infusion center under a restricted distribution program.¹ Due to the COVID-19 pandemic, there was concern for additional exposure of immunocompromised patients during health care facility visits. The manufacturer had obtained Food and Drug Administration (FDA) approval that temporarily permitted the infusion of natalizumab in the home under the TOUCH[®] Risk Evaluation and Mitigation Strategy (REMS) program.

Purpose

The study assessed the safety of natalizumab administration by comparing outcomes after receiving natalizumab infusions at home vs. infusion suites.

Methods

The study was a retrospective, non-inferiority multi-center chart review of patients receiving natalizumab in the home and outpatient infusion center. The primary outcome included safety (adverse events and infections), as assessed by pharmacist documentation. Non-inferiority was declared if the proportion of adverse events and infections for home infusion was no worse than the proportion for infusions performed in infusion suites, within statistical variability, by a margin of -3.0 percentage points. The study included MS patients over 18 years old prescribed natalizumab who have been treated for 6 consecutive uninterrupted natalizumab infusions prior to starting home infusion natalizumab. Exclusion criteria included natalizumab naive patients and patients receiving an MS concurrent therapy.

Results

Between May 4, 2020, and August 21, 2021, 7,699 natalizumab patients were screened based on referral information. Ninety-eight RRMS patients were randomly selected (natalizumab home infusion n=49 vs. natalizumab outpatient infusion n=49). Overall, there were no demographic differences between the 2 groups, other than female sex. Adverse events were reported in 6.1% (n=3) of the patients treated in an infusion suite and 8.2% (n=4) of patients treated in the home setting. There were no episodes of anaphylaxis, infections, unexpected toxicities, and no additional safety concerns identified.

Conclusion

The incidence of infusion-related events and adverse events was similar in both natalizumab groups. This retrospective study demonstrated a low incidence of adverse events in patients receiving natalizumab at home. These findings demonstrated that delivering natalizumab to patients who have received 6 consecutive uninterrupted infusions prior to starting home infusion natalizumab, is as safe as those who receive it in outpatient clinic. The convenience of the home setting should be considered in future care for immunocompromised patients. The results may be utilized in future studies to evaluate the safety of natalizumab infusions in the home setting. Furthermore, the framework of this study supports future studies to evaluate the safety of other monoclonal antibodies in the home setting.

Background

Multiple sclerosis (MS) is a progressive autoimmune inflammatory disorder causing demyelination and degeneration of the central nervous system, affecting 1 million people in the United States and about 2 million people worldwide.¹ Natalizumab is a highly effective monoclonal antibody therapy for the treatment of relapsing-remitting multiple sclerosis (RRMS).¹ It is usually delivered as 300 mg 1-hour intravenous infusion every 4 weeks.¹ Natalizumab is generally well tolerated by patients, however, the safety profile of natalizumab in long term can be associated with a rare brain infection called progressive multifocal leukoencephalopathy (PML). Because of the potential for infusion-related reactions of natalizumab and the risk of PML, it poses a great inconvenience to patients requiring them to receive the infusions in an authorized infusion center as part of a restricted distribution program called the TOUCH® Prescribing Program.¹ As part of the Coronavirus Disease 2019 (COVID-19) pandemic, patients and providers alike shared concerns about appointments in health care facilities that may increase immunocompromised patients' exposure risk to COVID-19. As such, the manufacturer had requested, and received U.S. Food and Drug Administration (FDA) advice that enabled the manufacture to temporarily offer in-home infusion of natalizumab for patients with RRMS under the TOUCH® REMS program during the COVID-19 Public Health Emergency. Previous studies in countries outside of the U.S., and therefore regulated under different drug safety authorities, have described natalizumab home infusion models with positive results in safety, outcomes, and patient satisfaction.^{2,3}

To support the provision of patient-centered care and provide home care as a safe option to patients with multiple sclerosis, it is necessary to develop a new model of care in the U.S. to deliver safe and effective therapy going forward.

Purpose

The study purpose was to assess the safety of natalizumab administration by comparing rate of infusion reactions and infections after receiving natalizumab infusions at home vs. outpatient clinics.

Methods

This study was a retrospective, multi-center chart review analysis of patients receiving natalizumab in the home and alternate infusion site. The primary

outcome included patient safety outcomes (adverse events and infections), as assessed by the information collected by pharmacists overseeing the care and dispensing for these patients. Study inclusion criteria included male and female patients over 18 years old diagnosed with MS who were prescribed natalizumab home infusions and have been treated for 6 consecutive uninterrupted infusions with natalizumab prior to starting home infusion natalizumab. The manufacturer has a shortened post-infusion observation period for those patients who have had ≥ 6 consecutive, uninterrupted natalizumab infusions (30 minutes vs. the current 60 minutes). Study exclusion criteria included naive patients who have never received natalizumab and were receiving a concurrent therapy. This study was deemed to be IRB exempt.

Statistical Analysis

Descriptive analyses of mean and standard deviation were reported for continuous variables and counts and frequency for dichotomous variables. Differences between continuous variables were calculated using Student's T test. Chi-square tests were performed when comparing dichotomous variables with cell sizes greater than $n=5$, and Fisher's Exact tests were performed when cell sizes were less than $n=5$.

Non-inferiority on the primary endpoint was determined using the confidence interval method, where the lower limit of the one-sided 97.5% confidence interval for the event rate in the investigational group versus the control group was greater than $m = -0.3$. Results of a power analysis showed that a sample size of 48 patients per study arm for a total of 96 was required to show non-inferiority at an alpha level of 0.025 with 80% power assuming that there is less than a 5% change in odds of adverse event between the control and treatment groups. All analysis was conducted using RStudio 2022.02.03 Build 492.

Results

Between May 4, 2020, and August 21, 2021, 7,699 patients were screened based on referral information received to the organization related to natalizumab at home and outpatient clinic infusions at 53 sites around the U.S. Ninety-eight patients were identified as meeting inclusion criteria (natalizumab home infusion $n=49$ vs. natalizumab outpatient infusion $n=49$). Overall, there were no statistically significant differences in demographics observed between the 2 treatment groups

as seen in Table 1. Most participants were female and had been receiving natalizumab over a mean of 3.7 years (home infusion) vs. 3.1 years (outpatient infusion). The mean age of participants was 43.3 years and 44.7 years in-home vs. clinic infusions, respectively. All were diagnosed as RRMS.

TABLE 1 | Summary of Baseline Patient Demographics for 98 Participants Receiving Natalizumab in Home vs. Outpatient Clinic

Variable	Home Infusion (n=49)	Outpatient Infusion (n=49)	Significance (p-value)
Age, mean (SD)	43.3 (10.4)	44.7 (11.1)	0.606
Gender			
Male, n (%)	14 (28.6%)	17 (34.7%)	0.664
Female, n (%)	35 (71.4%)	32 (65.31%)	
Years receiving natalizumab, mean (SD)	3.1 (1.8)	3.7 (2.8)	0.210

As shown in Figure 1, infusing natalizumab in the home setting was found to be non-inferior to infusions performed in an outpatient infusion center (OR=1.34, 95% CI: 0.217-9.780, m= -0.30). Events reported, as percentage, in patients receiving natalizumab at home included nausea/vomiting 2% (1), fatigue 2% (1), fever 2% (1), and arthralgia 2% (1). In outpatient clinic infusions, patients reported fatigue 2% (1), fever 2% (1), and arthralgia 2% (1). There were no episodes of anaphylaxis, infections, unexpected toxicities, and no additional safety concerns identified. There were no episodes or symptoms of PML observed in any of the patients.

Discussion

This retrospective study has demonstrated a low incidence of adverse events in patients receiving natalizumab at home. The study findings

demonstrated that delivering natalizumab to “expert patients” who have received 6 consecutive uninterrupted infusions with natalizumab prior to starting home infusion natalizumab, is as safe as those who receive it in outpatient clinic. The convenience of the location of delivery of safe treatments should be considered into future design of services for those immunocompromised such as multiple sclerosis patients. The data results, although specific to one organization, may be utilized in future studies to evaluate the safety of natalizumab infusions in the home setting. Furthermore, the framework of this study supports future potential studies to evaluate the safety of other outpatient monoclonal antibodies in the home setting.

Limitations of this study include potential for confounders that were not measured as well as possible selection bias. Another limitation is reliance on manual documentation for adverse event data.

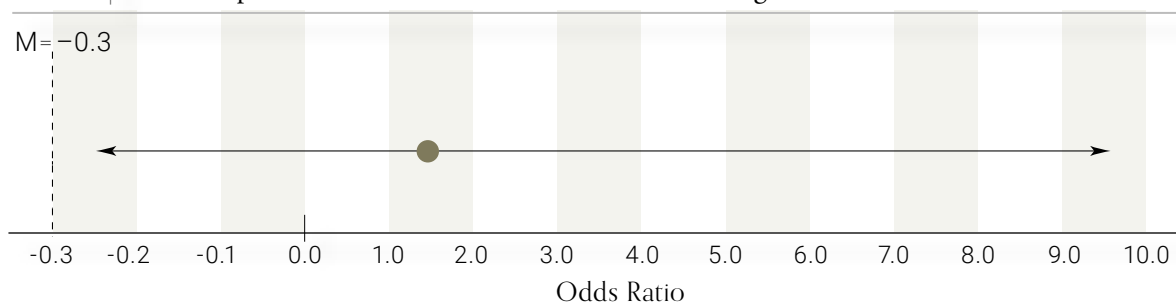
Conclusions

The incidence of infusion-related reactions was similar in both natalizumab infusions received at home and outpatient clinic. There was no difference in incidence of adverse events across both groups.

References

1. Tysabri (natalizumab) [prescribing information]. Cambridge, MA: Biogen Inc; June 2020.
2. Schultz TJ, Thomas A, Georgiou P, et al. Home infusions of natalizumab for people with multiple sclerosis: a pilot randomised crossover trial. *Ann Clin Transl Neurol.* 2021;8(8):1610-1621. doi:10.1002/acn3.51410.
3. Vijayan S, Adams J, Cook L, et al. Establishment of the first at-home natalizumab infusion service for the treatment of relapsing remitting multiple sclerosis (rmms). *Journal of Neurology, Neurosurgery & Psychiatry* 2017;88:e1.

FIGURE 1 | Non-Inferiority and Adverse Events for Infusion in an Outpatient Infusion Center versus a Home Setting



See you in Austin, TX

NHIA24

March 23 - 27, 2024



Sign up to be notified
when registration opens.

Baxter



AUTOMATED
COMPOUNDER



AMINO ACIDS



INFUSION PUMPS



VITAMINS

INFUSION
CLINICS



HOME
INFUSION



ADMINISTRATION SETS AND
NEEDLE-FREE CONNECTORS



PREMIXED DRUGS

LONG-TERM
CARE PHARMACY



AMBULATORY
SURGERY



IV SOLUTIONS



ANESTHESIA



GENERIC
INJECTABLES



HEMOSTATS AND
SURGICAL SEALANTS

IT'S ALL ABOUT CARE

EVERYWHERE CARE IS GIVEN

When looking for a trusted partner to provide the needed products to help care for your patients, Baxter is here. We've got you covered — from infusion pumps and administration sets, to premixed solutions for nutrition, intravenous therapies, surgical interventions and more. With over 90 years of experience, and a broad portfolio of products to support your therapeutic needs, our dedicated alternate site sales team is ready to help. ***We're where you need us.***

It's easy. Call 1-888-229-0001 or visit www.baxter.com

A Review of Daptomycin vs. Vancomycin for Susceptible Infections: Is One Superior for Outpatient Parenteral Antibiotic Treatment (OPAT)?

Daniel Decker
PharmD, MBA, BCACP
Option Care Health
dr.daniel.decker@
gmail.com

ABSTRACT

Background

Outpatient Parenteral Antibiotic Treatment (OPAT) is becoming a more frequent modality of completing a patient's antimicrobial treatment to save on hospitalization costs and decrease the risk of nosocomial infections. The use of vancomycin, a widely used medication in OPAT, may mitigate some of those savings due to dosing and lab monitoring challenges, adverse drug reactions (ADRs), clinical failure rate, and re-hospitalization risk associated with the drug. The objective of this review is to examine if daptomycin is a safer, more effective, and cost-saving medication to the health care continuum when used in the OPAT setting.

Methods

A literature review was conducted to evaluate the comparative rate of effectiveness, treatment failure due to adverse event (ADE), patient satisfaction, antimicrobial stewardship concerns, and potential cost comparisons of daptomycin and vancomycin.

Results

Daptomycin was shown to have a higher clinical success rate when used in OPAT vs. inpatient (94.6% vs. 86.3%) and a higher success rate vs. standard therapy for *S. aureus* when used in OPAT (90% vs. 83%). Compared to vancomycin, daptomycin decreased rate of clinical failure (OR 0.58), had a lower rate of discontinuation due to ADE (OR 0.15), less severe ADE, was associated with higher patient satisfaction, and is considered the superior treatment at a willingness to pay threshold above \$15,000 for severe infections.

Conclusion

According to the literature review, daptomycin may be superior to vancomycin for severe infections in the OPAT setting.

Key Words: *daptomycin, vancomycin, OPAT, AKI, WTP*

Introduction

The long duration of treatment necessary for severe infections and the high cost of inpatient hospital care have led insurance companies and health care providers to turn to outpatient parenteral antibiotic treatment (OPAT) to complete a patient's treatment course once they are stable for discharge. The global home infusion market, a large purveyor of OPAT, has an expected compound annual growth rate of 11% from 2021 through 2027, which has accelerated in recent years due to COVID shifting more care to the patient's home.¹ While OPAT adds significant cost savings, it is not without additional risks and challenges. When considering OPAT, all the risks of clinical failures are amplified as the patient is no longer in a hospital bed available for labs and doses at the provider's request. Therefore, patient compliance with dosing, labs, hydration, and other factors is paramount in determining clinical success or failure.

Vancomycin has been used for several decades in the hospital setting for parenteral treatment of severe gram-positive bacterial infections. While vancomycin's efficacy is still robust after many years, concerns about its toxicity, such as acute kidney injury (AKI), is often at the forefront of providers' minds. The risk of AKI increases with higher doses needed to obtain the necessary 15-20mg/L trough levels and durations longer than 2 weeks, which are frequently required to treat severe susceptible infections.²⁻⁴ *Cano et al.*, found that patients on vancomycin with a goal trough of 15-20mg/L for longer than 7 days increased their risk of AKI by 12% for every additional day they were treated.^{3,5} *Hidayat et al.* showed 30% of patients on high-dose vancomycin treated for greater than 2 weeks suffered nephrotoxicity.^{5,6} To minimize adverse effects and verify the drug concentration is appropriate for treatment, vancomycin has strict lab monitoring requirements depending on the method of dose monitoring, which places an additional cost, time, and convenience burden over other traditional antimicrobials. Despite AKI being a likely morbidity for many of these patients, vancomycin is one of the most common drugs infused in the home setting.^{7,8}

With a heightened focus on the cost of care, clinicians are faced with analyzing if a drug will be effective from both a clinical and a cost-effectiveness standpoint. To understand some of the possible cost impacts of vancomycin unrelated to the direct drug cost, *Jeffres*

analyzed the impact toxicities, lab costs, and provider time have on the health care continuum.⁹ From a toxicity standpoint, *Jeffres* noted that nephrotoxicity occurs on average within 4 to 17 days after the start of therapy and is highly correlated with higher doses, length of therapy >7 days, and patients receiving additional nephrotoxic drugs.^{9,10} These factors can significantly increase the hospital length of stay (LOS) by 3.5 to 15 days (depending on the study and hospital ward) which also increases total medical cost (17.7% - 23.9%).^{4,9} Monitoring vancomycin levels and dosing vancomycin can also be costly, as patients can require lab draws up to biweekly depending on their acuity and risk factors which have associated lab-related costs and nursing time. Additionally, if providers wish to follow the 2019 Infectious Diseases Society of America (IDSA) guidelines and use the recommended area-under-the-curve (AUC) dosing instead of trough-based dosing, their choices are additional lab draws needed for the calculation or the use of software with Bayesian modeling, which can cost an organization tens of thousands of dollars per year.^{9,11,12} *Jeffres* also found that the mean cost to prevent 1 episode of vancomycin-related nephrotoxicity is \$25,167, and the cost to treat said nephrotoxicity is \$11,234.⁹ When totaled, this comes to a willingness to pay (WTP) to avoid 1 episode of vancomycin-related nephrotoxicity of approximately \$40,000, which was corroborated in a cost-effectiveness analysis performed in 2021 by *Vu et al.*¹³ Most of these costs could be eliminated or reduced by using alternative antimicrobials.

Since administering vancomycin safely poses many challenges, clinicians have looked for alternatives that may simplify the infusion process while adequately treating the patient's condition and preventing readmission. Daptomycin, a lipopeptide antibiotic released under the trade name Cubicin® in 2003, is used to treat infections resistant to vancomycin but also shares a similar efficacy profile for gram-positive bacterial infections such as methicillin-resistant *Staphylococcus aureus* (MRSA).^{8,14} With its once-daily dosing, lower rate of serious adverse drugs events (ADEs), less stringent lab monitoring requirements, and dosing that is less likely to require titration, daptomycin is often viewed as a safer, less complicated alternative which may decrease overall costs to the health care continuum while preserving clinical outcomes.^{2,14,15} However, the higher drug cost of daptomycin, which can be a multiple of 4 to 12x

the cost of vancomycin, and inpatient antimicrobial stewardship ideology have been barriers to more frequent use.¹⁶

The objective of this review is to analyze the available literature comparing clinical outcomes due to treatment failure, failure due to ADEs, ease of use, and patient satisfaction as possible contributors for clinical failure. Additionally, this study seeks to assess the total costs associated with treatment for both medications reflecting the cost burden clinical failures have on the health care continuum. Finally, this review will discuss which antimicrobial has a stronger case for use in OPAT regarding the challenges associated with therapy in this setting.

Methods

A literature search was conducted using the University of Florida online library Primo search function and Google Scholar from 2007 through 2022, emphasizing literature published since 2012 with full text copies available.

The following search terms were used: “vancomycin,” “daptomycin,” “opat,” “copat,” “mrsa,” and “cost” in a variety of and/or combinations. A bibliography search was conducted to obtain additional resources.

Results

Clinical Efficacy and Effectiveness

Many studies have tried to capture various facets of clinical effectiveness by analyzing clinical failure rates and reasons for clinical failure. A significant contributor to clinical failure is the early discontinuation of an antimicrobial due to an ADE. *Maraolo et al.* noted in their meta-analysis comparing daptomycin and vancomycin for the treatment of MRSA bloodstream infections with or without endocarditis that daptomycin had an odds ratio of 0.15 compared to vancomycin for discontinuation due to adverse effects.¹⁷ Additionally, no significant difference in mortality but a significantly lower risk of clinical failure (OR 0.58) was found for daptomycin.¹⁷

Daptomycin has also been shown to have a higher success rate in the OPAT versus institutional setting. Results from the Cubicin Outcomes Registry and Experience (CORE), which was a post-marketing analysis, demonstrated that the clinical success rate of daptomycin in OPAT exceeded its inpatient success rate of 94.6% to 86.3% ($p < 0.001$), respectively.¹⁸ *Rehm et al.* showed a clinical success rate of 90% vs. 83% for daptomycin compared to standard therapy

for *S. aureus* infections in OPAT.¹⁹ Daptomycin also demonstrated a lower infection relapse rate (3.9% vs. 15.5%, $p = 0.007$), a lower mortality rate 6 weeks after completion of therapy (3.9% vs. 18.6%, $p = 0.001$), and a much higher clinical success rate over inpatient antibiotic therapy (86.4% vs. 55.7%, $p < 0.001$) vs. standard of care.¹⁹ *Seaton et al.* corroborated these results, analyzing the European Registry for daptomycin usage in OPAT and showing an 89% clinical success rate over a wide range of susceptible infections.²⁰ Noteworthy for these studies was that OPAT patients tended to be younger and have fewer comorbidities when compared with those who finished their therapy in the hospital; however, these factors are unlikely to favor one therapy over another for OPAT but more likely to impact the decision to service the patient institutionally or via OPAT.¹⁸⁻²⁰ This insinuates that while it is considered at least as effective as vancomycin in the hospital setting, data suggests better efficacy when used in the less controlled environment of OPAT.

While treatment failure from an ADE is a concern from an inpatient perspective, it is an even greater concern in OPAT due to the increased possibility of treatment failure. *Shrestha et al.* analyzed a single center cohort receiving vancomycin and daptomycin over a 3-year period to compare adverse events, health care interventions, and health care utilization during their OPAT course, which was standardized to a rate per 1,000 OPAT days.⁸ It was determined that vancomycin had more than double the ADE rate ($p = 0.02$) and 4.8x the rate of antimicrobial interventions ($p < 0.001$) than daptomycin patients.⁸ *Schrank et al.* conducted a retrospective analysis among OPAT patients receiving vancomycin vs. daptomycin over a 3-year period analyzing change or discontinuation of antimicrobial due to an ADE occurring greater than 7 days prior to the end of therapy.¹⁵ After adjusting for multiple differences in patient population characteristics, the ADE rate leading to a change or early discontinuation of treatment was 19.0% vs. 7.6% ($p < 0.01$) for vancomycin and daptomycin respectively, which typically would happen earlier in the treatment course ($p < 0.01$) for vancomycin.¹⁵ Additionally, the vancomycin group was 3.7x more likely to have an ADE (OR = 3.71, $p < 0.01$) related to discontinuation of treatment than the daptomycin group.¹⁵ The severity of ADE was notable, with the vancomycin group's most prevalent ADE being renal involvement (32% of ADE, 6% of patients overall), hypersensitivity

reactions (22% of ADE, 4.2% of patients overall), and cytopenias (10% of ADE, 1.9% of patients overall), vs. asymptomatic CK elevation of a 10-fold increase above the upper normal limit (50% of ADE, 4% of patients overall) and rhabdomyolysis (38% of ADE, 3% of patients overall) for daptomycin.^{14,15} A confounder mentioned by the authors was a significant difference in the location of OPAT, with significantly more patients on vancomycin receiving treatment in a long-term acute or skilled nursing facility ($p < 0.01$).¹⁵ This population tended to have a higher burden of comorbidities which could contribute to a higher likelihood of ADE.¹⁵ However, this population had a lower risk of medication changes due to ADE which may be explained by quicker access to hydration and the availability of hypersensitivity reaction abortive medications, which may have prevented a medication change.¹⁵ While these results are higher than the discontinuation rate of daptomycin documented in the European Registry, showing 3.1% of patients discontinued treatment related to ADE, daptomycin still demonstrates advantages over vancomycin regarding ADE.²⁰

Patient Adherence and Contributing Factors to Treatment Success

Often overlooked facets of OPAT outcomes include patient adherence, satisfaction, and perceived burden on their daily life. *Neiman et al.* noted that half of prescribed medications are taken incorrectly with regards to timing, dosage, frequency, and duration, which has a significant impact on treatment success, hospital readmission, and cost of care.²¹ *Wu et al.* assessed some of these issues by conducting a short telephone survey with patients treated with daptomycin or vancomycin to assess the impact on a patient's daily routine, ADE, hospital readmission, and time off work, which was collated into a daily impact score.²² Patients received daptomycin every 24 hours, while vancomycin patients received doses ranging from every 8 hours to every 48 hours, with every 12 hours being the most prevalent.²² The results demonstrated a higher daily impact score for vancomycin patients and a higher overall subjective satisfaction with daptomycin over vancomycin therapy (100% vs. 67% rated satisfaction of 8/10 or better on a 0-10 rating scale, respectively) which may be attributed to vancomycin infusions having a more varied frequency schedule along with 1-2 hours per infusion vs. once-daily dosing of daptomycin which is infused in 30 minutes or less.^{2,14,21} Patient perceived daily impact of therapy and patient

adherence to therapy could contribute to a much higher completion rate of daptomycin OPAT therapy vs. standard of care noted by *Rehm et al.* showing a 90.3% vs. 45.4% ($p < 0.001$) respectively.¹⁹

The antimicrobial stewardship community has taken note of this nuance as it demonstrates the difference between antimicrobial stewardship in the inpatient realm vs. OPAT. The usual doctrine of the antimicrobial stewardship community is the desire to preserve the efficacy of newer, novel, or broader-spectrum treatments by using older, more established treatments first, reserving the newer treatments for use only when initial treatment has failed.¹⁶ This would favor vancomycin over daptomycin, which is evident in many hospitals' treatment protocols. However, *Mahoney et al.* addressed this stating that while a narrower-spectrum agent over a broader one may be a priority in the inpatient setting, the OPAT setting focuses on ease of administration and convenience which are factors that can affect patient adherence, completion of therapy, and antimicrobial resistance in the community setting.¹⁶

Total Health Care Costs

Several authors endeavored to quantify the economic benefit of using various MRSA-focused antimicrobials to determine whether there is an advantage of using one over another. *Patel et al.* attempted to create an economic model which included a cost-minimization and cost-effectiveness analysis of daptomycin, vancomycin, and linezolid for MRSA acute bacterial skin and skin structure infections (ABSSSI) for which institutional and OPAT direct costs were included.²³ While they concluded vancomycin was significantly more cost-effective than daptomycin (18.5% lower cost of treatment), some limitations significantly favored vancomycin.²³ In the base-case and the scenario 1 sensitivity analysis, they assumed the same LOS regardless of the drug, which can be refuted by multiple studies that show daptomycin has a shorter time to clinical success.²³ Additionally, the scenario 3 sensitivity analysis used efficacy rate instead of clinical success rate (effectiveness), which would include treatment failures from ADE.²³ Since they included OPAT in this analysis, the clinical success rate would have been a better surrogate for real-world scenarios, as ADE have a large impact on patients completing a course of antimicrobials. Finally, the authors analyzed vancomycin ADE cost impact during the first 3 days of treatment (empiric phase) which increased the

favorability of vancomycin since studies have shown the longer a patient is on vancomycin, the more likely they are to have an ADE.^{6,23}

While the data is mixed on which is superior for ABSSSI due to the shorter duration of treatment and lower drug level targets needed, data analyzing more severe infections requiring a longer duration of treatment paints a different picture. *Vu et al.* completed an exploratory cost-effectiveness analysis that compared daptomycin and vancomycin for MRSA bloodstream infections in Veterans Health Administration patients.¹³ Patients remained hospitalized until response or microbiological failure, which required an additional 14 days of salvage treatment.¹³ Patients who were discharged received OPAT for 21 days.¹³ Primary outcomes measured were microbiological failure within the first 7 days of treatment and ADE-related treatment failure after 7 days of treatment added together as a composite.¹³ Cost-effectiveness was analyzed using incremental cost-effectiveness ratios (ICER) with a WTP threshold of \$40,000 to avoid 1 clinical failure.¹³ In the 4-week and 6-week treatment analyses, daptomycin was a more expensive and effective than vancomycin.¹³ A probabilistic sensitivity analysis was conducted using 10,000 iterations via a Monte-Carlo simulation with varying parameters of the stratified primary endpoints demonstrating that at a \$40,000 WTP threshold, daptomycin, vancomycin, and other treatments were favored 50%, 31%, and 19% of the time respectively.¹³ When the WTP is varied, daptomycin was favored over vancomycin most of the time at any WTP >\$15,000, significantly lower than the cost a vancomycin failure (\$40,000) has on the health care continuum.¹³ Some limitations of this analysis are the predominantly male population and the costs used for this study, which are comparable to 340B drug prices to which only a small group of health care facilities have access. The direct drug cost savings, particularly on daptomycin, would be substantial and could impact this analysis if applied to other health systems or OPAT providers. Table 1 lists the studies analyzed and provides an overview of the data.

Discussion

From the approval of daptomycin in 2003, it can be determined that it is non-inferior to vancomycin for susceptible infections. However, when looking at the overall effectiveness of treatment, daptomycin had a much higher clinical success rate due to better tolerability, lower rate of therapy-ending ADE,

shorter infusion time, less frequent dosing, and ease of dosing leading to higher patient satisfaction, mainly when the OPAT setting was included in the analysis. The one clinical area where the data does not strongly favor daptomycin for effectiveness is for less severe infections such as ABSSSI or urinary tract infection (UTI). The reasons for this are evident as lower doses and shorter treatment durations significantly decrease the likelihood of a therapy-ending ADE or clinical failure for vancomycin. In addition, patient satisfaction is less likely to be a barrier as the shorter duration of treatment would impact a patient's life for a shorter period. Since this would lead to a lower rate of treatment failure for vancomycin, the cost-benefit profile would favor vancomycin and make it the superior agent for use in the short term, less severe infections.

The 2 areas that were up for debate prior to this analysis were the antimicrobial stewardship angle and the total cost of treatment for severe infections requiring higher doses of vancomycin and a longer treatment timeline. The article by *Mahoney et al.* addresses stewardship illustrating that the focus for antimicrobial stewardship in OPAT is patients taking a drug correctly and completing therapy as those can also impact antimicrobial resistance.¹⁶ From a total cost of treatment standpoint, the data for longer treatment courses may favor daptomycin for OPAT. *Vu et al.* stated that daptomycin is favored more often than other agents against MRSA at a WTP of \$15,000.¹³ Considering the WTP to avoid a vancomycin-induced AKI is about \$40,000, this makes a compelling case for the use of daptomycin.

There are some limitations to the available data to make a concrete determination of superiority. First, there is no data on vancomycin-induced AKI strictly in the OPAT setting. There are theoretical reasons why it could be higher in the OPAT vs. inpatient setting, but there are no studies focusing on this specifically. With that data point, the rate can be assumed from prior studies, most of which took place in the institutional setting. Second, all these studies were done with trough-based dosing of vancomycin. AUC-based dosing has shown to decrease the risk of AKI by 50% which could significantly change the treatment failure rate of vancomycin due to ADE.¹¹ Finally, a cost-benefit analysis would also need to be done on Bayesian software, an often-used method for AUC calculations. *Jeffres* noted that a pharmacist,

TABLE 1 | Overview of the Reviewed Studies

Author	Title	Study Sample Size	Summary
<i>Maraolo et al.</i>	Daptomycin versus vancomycin for the treatment of methicillin-resistant <i>Staphylococcus aureus</i> bloodstream infection with or without endocarditis: a systematic review and meta-analysis	1,226 patients, 554 vs. 672 in daptomycin vs. vancomycin, respectively	Risk of clinical failure of Daptomycin vs. Vancomycin = OR 0.58. Discontinuation of medication due to adverse effects of Daptomycin vs. Vancomycin = OR 0.15. Mortality of Daptomycin vs. Vancomycin patients = OR 0.73 (not statistically significant)
<i>Nathwani D. via CORE trial</i>	Developments in outpatient parenteral antimicrobial therapy (OPAT) for gram-positive infections in Europe, and the potential impact of daptomycin	1,160 patients treated with daptomycin for susceptible infections	Clinical success rate inpatient = 86.3%, Clinical success rate outpatient = 94.6%
<i>Rehm et al.</i>	Community-based outpatient parenteral antimicrobial therapy (Copat) for <i>Staphylococcus aureus</i> bacteraemia with or without infective endocarditis: analysis of the randomized trial comparing daptomycin with standard therapy	200 patients, 103 daptomycin, 97 with standard of care (SoC)	Daptomycin clinical success rate = 90%. Semi-synthetic penicillin or vancomycin + gentamicin (SoC) = 83%. Infection relapse rate: daptomycin = 3.9%, SoC = 15.5%. Mortality rate 6 weeks after completion of therapy: daptomycin = 3.9%, SoC = 18.6%. Completion rate of daptomycin vs. vancomycin = 90.3% vs. 45.4%
<i>Seaton et al.</i>	Daptomycin for outpatient parenteral antibiotic therapy: A European Registry experience (EU-CORE)	550 patients received daptomycin OPAT	The overall clinical success of daptomycin over susceptible infections for OPAT = 89%
<i>Shrestha et al.</i>	Adverse events, health care interventions, and health care utilization during home infusion therapy with daptomycin and vancomycin: a propensity score-matched cohort study	119 daptomycin, 357 vancomycin	ADE rate 3.2 vs. 7.7 events per 1,000 OPAT days, 5.6 vs. 27.1 antimicrobial interventions per 1,000 OPAT days for daptomycin vs. vancomycin, respectively
<i>Schrank et al.</i>	A retrospective analysis of adverse events among patients receiving daptomycin versus vancomycin during outpatient parenteral antimicrobial therapy	105 daptomycin, 312 vancomycin	ADE leading to change or early discontinuation of treatment 7.6% vs. 19% daptomycin vs. vancomycin, respectively. aOR = 3.71 for the incidence of ADE for vancomycin over daptomycin
<i>Patel et al.</i>	Economic burden of inpatient and outpatient antibiotic treatment for methicillin-resistant <i>Staphylococcus aureus</i> complicated skin and soft-tissue infections: a comparison of linezolid, vancomycin, and daptomycin.	Cost per patient based on 7 to 14 days of treatment	Total cost of treatment: daptomycin = \$13,612, vancomycin = \$11,096. Gain in QALYs for daptomycin over vancomycin-treated patients = 0.001 QALY
<i>Vu et al.</i>	Exploratory cost-effectiveness analysis for treatment of methicillin-resistant <i>Staphylococcus aureus</i> bloodstream infections: Is linezolid or daptomycin favored over vancomycin?	Cost per patient for 4 and 6 week regimens with probabilistic sensitivity analysis, including 10,000 iterations via Monte-Carlo simulation	Daptomycin dominated vancomycin at 4 and 6 weeks of treatment. Sensitivity analysis: Daptomycin, vancomycin, and linezolid were favored in 50%, 31%, and 17% of 4-week probabilistic iterations, respectively, at \$40,000 WTP.

on average, takes about 40 minutes to evaluate patients regarding pharmacokinetic evaluation, interpret results, and follow-up with the patient.⁹ The possible decrease in provider time cost vs. the cost of using the software would have to be assessed to see how this would affect the total cost of treatment.

Many of the cost analyses conducted either occurred prior to the introduction of generic daptomycin to the market or were completed in a setting where the cost does not reflect what most health systems or purveyors of OPAT would pay. Therefore, a study using non-government priced drugs would need to be performed with costs extrapolated to the present day to best quantify if there are any differences. In addition, the acute nature of treatment with these drugs makes pharmacoeconomic analysis, such as cost-effectiveness or cost-utility analysis, difficult as these analyses are usually performed on chronic conditions with a long duration of therapy. When *Patel et al.* attempted a cost-effectiveness analysis on vancomycin and daptomycin for MRSA ABSSSI, they showed a difference of 0.001 QALY (8.8 quality-adjusted life hours), which is not likely to sway an argument toward one medication or another.²³ Finally, there are no studies analyzing the societal costs of using vancomycin in the OPAT setting. With more frequent, longer dosing requirements, up to biweekly lab monitoring, and the possibility of renal failure, which could cause an additional hospitalization and longer courses of antimicrobial treatment, this can impact the patient's time away from work decreasing their productivity and productivity of family members supporting the patient during their treatment.

Conclusion

With an efficacy rate that is non-inferior to vancomycin, an effectiveness rate that may be superior to vancomycin in the OPAT setting, a lower risk of ADE, simplified lab requirements and dosing, and a likely cost-benefit to the health care continuum for longer-term therapy, daptomycin may be superior to vancomycin for use in severe infections in the OPAT setting. However, further studies are needed in the OPAT setting to address rate of ADE and costs.

Funding: No funding was received for this manuscript

References

1. Global Market Insights Inc. 2022. Home Infusion Therapy Market Size, Forecast Report 2021-2027. [online] Available at: <<https://www.gminsights.com/industry-analysis/home-infusion-therapy-market-report>> [Accessed 1 July 2022].
2. Accessdata.fda.gov. 2022. [online] Available at: <https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/060180s047lbl.pdf> [Accessed 10 July 2022].
3. Cano EL, Haque NZ, Welch VL, et al. Incidence of nephrotoxicity and association with vancomycin use in intensive care unit patients with pneumonia: retrospective analysis of the IMPACT-HAP Database. *Clin Ther.* 2012;34(1):149-157.
4. 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. *Clin Infect Dis.* 2011;52(3):e18-55.
5. Bamgbola O. Review of vancomycin-induced renal toxicity: an update. *Ther Adv Endocrinol Metab.* 2016;7(3):136-147.
6. Hidayat LK, Hsu DI, Quist R, Shriner KA, Wong-Beringer A. High-dose vancomycin therapy for methicillin-resistant *Staphylococcus aureus* infections: efficacy and toxicity. *Arch Intern Med.* 2006;166(19):2138.
7. Rochesterhomeinfusion.com. 2022. Anti-Infectives | IV Therapy Services | In Home IV Treatment. [online] Available at: <<https://www.rochesterhomeinfusion.com/services/anti-infective.html>> [Accessed 2 July 2022].
8. Shrestha NK, Mason P, Gordon SM, et al. Adverse events, healthcare interventions and healthcare utilization during home infusion therapy with daptomycin and vancomycin: a propensity score-matched cohort study. *Journal of Antimicrobial Chemotherapy.* 2014;69(5):1407-1415
9. Jeffres MN. The whole price of vancomycin: toxicities, troughs, and time. *Drugs.* 2017;77(11):1143-1154.
10. van Hal SJ, Paterson DL, Lodise TP. Systematic review and meta-analysis of vancomycin-induced nephrotoxicity associated with dosing schedules that maintain troughs between 15 and 20 milligrams per liter. *Antimicrob Agents Chemother.* 2013;57(2):734-744.
11. Rybak MJ, Le J, Lodise TP, Levine DP, Bradley JS, Liu C, Mueller BA, Pai MP, Wong-Beringer A, Rotschafer JC, Rodvold KA, Maples HD, Lomaestro BM. Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: A revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. *Am J Health Syst Pharm.* 2020 May 19;77(11):835-864. doi: 10.1093/ajhp/zxaa036. PMID: 32191793.
12. Lee BV, Fong G, Bolaris M, et al. Cost-benefit analysis comparing trough, two-level AUC and Bayesian AUC dosing for vancomycin. *Clin Microbiol Infect.* 2021;27(9):1346.e1-1346.e7.
13. Vu, M., Smith, K.J., Aspinall, S.L. et al. Exploratory Cost-Effectiveness Analysis for Treatment of Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections: Is Linezolid or Daptomycin Favored Over Vancomycin? *Clin Drug Investig* 41, 885–894 (2021). <https://doi.org/10.1007/s40261-021-01077-8>
14. Merck.com. 2022. [online] Available at: <https://www.merck.com/product/usa/pi_circulars/c/cubicin/cubicin_pi.pdf> [Accessed 2 July 2022].
15. Schrank GM, Wright SB, Branch-Elliman W, LaSalvia MT. A retrospective analysis of adverse events among patients receiving daptomycin versus vancomycin during outpatient parenteral antimicrobial therapy. *Infect Control Hosp Epidemiol.* 2018;39(8):947-954.

16. Mahoney, M.V., Childs-Kean, L.M., Khan, P. et al. Recent Updates in Antimicrobial Stewardship in Outpatient Parenteral Antimicrobial Therapy. *Curr Infect Dis Rep* 23, 24 (2021).
17. Maraolo AE, Giaccone A, Gentile I, Saracino A, Bavaro DF. Daptomycin versus vancomycin for the treatment of methicillin-resistant staphylococcus aureus bloodstream infection with or without endocarditis: a systematic review and meta-analysis. *Antibiotics (Basel)*. 2021;10(8):1014.
18. Nathwani D. Developments in outpatient parenteral antimicrobial therapy (Opat) for Gram-positive infections in Europe, and the potential impact of daptomycin. *J Antimicrob Chemother*. 2009;64(3):447-453.
19. Rehm S, Campion M, Katz DE, Russo R, Boucher HW. Community-based outpatient parenteral antimicrobial therapy (Copat) for Staphylococcus aureus bacteraemia with or without infective endocarditis: analysis of the randomized trial comparing daptomycin with standard therapy. *J Antimicrob Chemother*. 2009;63(5):1034-1042.
20. Seaton RA, Gonzalez-Ramallo VJ, Prisco V, et al. Daptomycin for outpatient parenteral antibiotic therapy: a European registry experience. *Int J Antimicrob Agents*. 2013;41(5):468-472.
21. Neiman AB, Ruppert T, Ho M, et al. CDC Grand Rounds: Improving Medication Adherence for Chronic Disease Management — Innovations and Opportunities. *MMWR Morb Mortal Wkly Rep* 2017;66. DOI: <http://dx.doi.org/10.15585/mmwr.mm6645a2>.
22. Wu KH, Sakoulas G, Geriak M. Vancomycin or daptomycin for outpatient parenteral antibiotic therapy: does it make a difference in patient satisfaction? *Open Forum Infectious Diseases*. 2021;8(8):ofab418.
23. Patel D, Stephens J, Gao X, Verheggen, Shelbaya A, Haider S. Economic burden of inpatient and outpatient antibiotic treatment for methicillin-resistant Staphylococcus aureus complicated skin and soft-tissue infections: a comparison of linezolid, vancomycin, and daptomycin. *CEOR*. Published online September 2013:447.

Call for Manuscripts

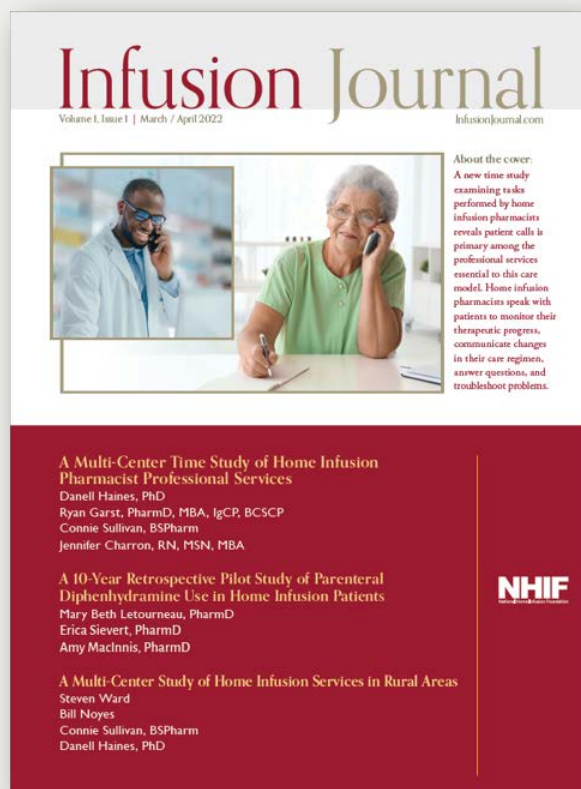
Study, share, and learn

Home and alternate site infusion providers have access to extensive data and unique context, but they lacked a journal to foster the orderly communication of the information—until now!

Infusion Journal provides an outlet for communicating research in a formal and validated way. By publishing on topics relevant to infusion therapy administered in the home, clinic, suite, or other setting, the industry can share information that creates a foundation for advancement by documenting achievements, identifying areas for improvement, and generating new ideas.

Now accepting:

- Independent original research studies
- Case studies
- Health economic analyses
- Therapy updates
- Clinical consultations
- Commentary



All manuscripts undergo peer review

Authors adhere to strict, established ethical standards

To learn more, go to www.nhia.org/nhif/infusion-journal
or contact Michelle.Simpson@NHIA.org

Guidelines for Writing Case Reports for *Infusion Journal*

Why

One report is an event; 2 are a coincidence, and a third is a potential association. Case reports are one of the most relevant types of manuscripts. A PubMed analysis of a 30-year span (1991-2020) found more than 1 million articles of primary literature, with case reports representing 27.54%.¹ Case reports describe new diseases or disease mechanisms, therapeutic approaches, and adverse or beneficial effects of drugs. They are short communications intended to share experiences with an interesting or unusual patient case. A case report tells a real-world story that can be applied to similar scenarios. If applied and the outcome is repeated, it leads to further evaluation and larger study designs.

Clinicians will use case reports to direct the care provided to patients, including home infusion patients. Case reports can offer solutions to individualized problems when dealing with rare diseases or new medications. Home infusion professionals regularly receive prescriptions for off-label indications or medication doses, and they may find the only information supporting it is a single case report.

Infusion Journal wants to publish case reports from home infusion professionals. When you are collaborating and solving potential barriers to onboarding a patient to home infusion services, those innovations can be written into a case report. The patient with a specific reason for previously being ineligible for home infusion might be the case report that raises awareness of a protocol to safely manage other patients with the same issue.

Case reports are shorter and easier to write than other types of manuscripts. The focus is on an exceptional patient situation and discusses it in detail, adding a literature review to the topic. Authors should write about why the main message is important and provide descriptions of the symptoms, signs, diagnosis, treatment, or follow-up of an individual patient. Well-written and transparent case reports reveal early signals of potential benefits, harms, and information on the

use of resources; provide information for clinical research and clinical practice guidelines; and inform medical education.²

How

A case report tells a story in a narrative format covering clinical findings, diagnoses, interventions, outcomes, and follow-up. Case reports support clinical research with evidence from episodes of care. The development of case reporting guidelines has improved the communication of this valuable type of research.² When written with reporting guidelines, case reports provide comprehensive information related to clinical management, leading to further study, replication, and transparency.

Infusion Journal accepts submissions of Case Reports for publication and requests authors follow *Case Reporting (CARE) Guidelines for Case Reports* developed by a consensus group to support the publication of accurate, complete, and transparent case reports (see the checklist on next page).²

The home setting for infusion medications offers an ample supply of topics for interesting and unique patient cases to report. If you have a patient case or idea for writing a case report or questions about submitting a manuscript to *Infusion Journal*, contact: infusionjournal@nhia.org.

References

1. Zhao X, Jiang H, Yin J, Liu H, Zhu R, Mei S, et al. Changing trends in clinical research literature on PubMed database from 1991 to 2020. *European Journal of Medical Research*. 2022;27(1). doi: 10.1186/s40001-022-00717-9.
2. Riley DS, Barber MS, Kienle GS, Aronson JK, Von Schoen-Angerer T, Tugwell P, et al. CARE guidelines for case reports: explanation and elaboration document. *Journal of Clinical Epidemiology*. 2017;89:218-35. doi: 10.1016/j.jclinepi.2017.04.026.
3. CARE Checklist of Information to Include when writing a case report. 2013. Case Report Guidelines. CARE Statement. <https://www.care-statement.org/checklist>. Accessed January 15, 2023.

Checklist of Information to Include in Written Case Reports³

Item	Description of Item and Information to Include
Title	The diagnosis or intervention of primary focus followed by the words “case report”
Key Words	2 - 5 key words that identify diagnoses or interventions in this case report
Abstract	<ul style="list-style-type: none"> • Introduction – What is unique, and what does it add to the scientific literature? • The patient’s main concerns and important clinical findings • The primary diagnoses, interventions, and outcomes • Conclusion – What are one or more “take-away” lessons from this case report?
Patient Information	<ul style="list-style-type: none"> • De-identified patient-specific information • Primary concerns and symptoms of the patient • Medical, family, and psychosocial history, including relevant genetic information • Relevant past interventions and their outcomes
Clinical Findings	Describe significant physical examination and important clinical findings.
Timeline	Historical and current information from this episode of care organized as a timeline
Diagnostic Assessment	<ul style="list-style-type: none"> • Diagnostic methods (physical exam, laboratory testing, imaging, surveys) • Diagnostic challenges • Diagnosis (including other diagnoses considered) • Prognostic characteristics when applicable
Therapeutic Intervention	<ul style="list-style-type: none"> • Types of therapeutic intervention (pharmacologic, surgical, preventive) • Administration of therapeutic intervention (dosage, strength, duration) • Changes in therapeutic interventions with explanations
Outcomes	<ul style="list-style-type: none"> • Clinician- and patient-assessed outcomes if available • Important follow-up diagnostic and other test results • Intervention adherence and tolerability (How was this assessed?) • Adverse and unanticipated events
Discussion	<ul style="list-style-type: none"> • Strengths and limitations in your approach to this case • Discussion of the relevant medical literature • The rationale for your conclusions • The primary “take-away” lessons from this case report in a one paragraph conclusion
Patient Perspective	The patient should share their perspective on the treatment(s) they received.
Informed Consent	The patient should give informed consent.

Successful Transition from Subcutaneous Immune Globulin (SCIG) Therapy to Intravenous Immune Globulin (IVIg) Therapy in Primary Immunodeficiency: A Case Report

Amy Mulgrew
RN, CRNI, IgCN, VA-BC
Advanced Infusion Care

Ashley McKenna
RN, IgCN
Advanced Infusion Care

Erin Mullis
RN, IgCN
Advanced Infusion Care

Lead author contact:
amulgrew@aiscaregroup.com

ABSTRACT

For patients with primary immunodeficiency (PI), immune globulin (Ig) is a lifelong therapy. This specialized infusion therapy is a safe and practical option for patients to receive in the comfort of their own homes. Intravenous immune globulin (IVIg) and subcutaneous immune globulin (SCIG) are clinically proven effective treatments for PI and offer distinct advantages and disadvantages for each route of administration.

Using patient characteristics to help guide decisions for intravenous or subcutaneous treatment, Ig therapy must be individualized to meet each patient's specific clinical needs with consideration for patient preferences.

The following patient case report describes a successful transition from SCIG to IVIg therapy, emphasizing the importance of patient choice and individualization of treatment.

Keywords: *chronic variable immunodeficiency, subcutaneous immune globulin, intravenous immune globulin*

Introduction

For patients with primary immunodeficiency (PI), immune globulin (Ig) is a lifelong therapy. This specialized infusion therapy is a safe and practical option for patients to receive in the comfort of their own homes. Intravenous immune globulin (IVIg) and subcutaneous immune globulin (SCIG) are clinically proven effective treatments for PI and offer distinct advantages and disadvantages for each route of administration.

Using patient characteristics to help guide decisions for intravenous or subcutaneous treatment, Ig therapy must be individualized to meet each patient's specific clinical needs with consideration for patient preferences.

The following patient case report describes a successful transition from SCIG to IVIg therapy, emphasizing the importance of patient choice and individualization of treatment.

Patient Case Presentation

In 2015, a male in his 30s diagnosed with chronic variable immunodeficiency (CVID), 1 of the more than 400 types of PI, presented to our services for home infusion of IVIG. During his treatment from 2015-2020, the monthly IVIG infusions were generally well tolerated, with no reports of severe adverse drug reactions (ADRs) or hospitalization related to home infusion therapy. The patient's IVIG treatments included premedication with orally administered acetaminophen 650 mg and diphenhydramine 25 mg. After the first dose, hydration was added to the patient's treatment plan to be administered post infusion. He received sodium chloride 0.9% 500 mL administered intravenously. Throughout treatment, the patient reported mild ADRs described as fatigue and lethargy during the infusion and for 36 hours post-infusion.

In 2020, the patient requested a transition from IVIG to SCIG to determine if SCIG could effectively treat his CVID without the ADRs he experienced using IVIG. As a result, the patient received SCIG 20% 10 gm weekly (40 grams per month, 504 mg/kg/month). In addition, before each SCIG infusion, the patient received acetaminophen 650 mg and diphenhydramine 25 mg orally to prevent and treat SCIG ADRs.

In late 2021, the patient noted numerous ADRs from his weekly SCIG infusions and stated he felt better on the monthly infusion of IVIG. The patient's ADR list from SCIG included significant local swelling and pain, fatigue, lethargy, and complaints of back pain after each SC infusion. The ADRs were evaluated, and adjustments were made to slow the infusion. Additionally, the pharmacy changed the needle length from 9 mm to 12 mm to decrease local site reactions and ensure the distribution of Ig medication within the subcutaneous tissue. Despite making adjustments to eliminate or minimize the localized ADRs, the patient discussed a treatment plan with his prescriber to transition from weekly SCIG back to monthly IVIG infusions.

In December 2021, the patient was transitioned to IVIG 10% 30 gm every 4 weeks (357 mg/kg/4 weeks), administering the same brand of IVIG product previously used for IVIG treatment. He continued oral premedication with acetaminophen 650 mg and diphenhydramine 25 mg.

Serum level monitoring of IgG reported: 494 mg/dL (March 2016), 823 mg/dL (April 2021), 1283 mg/dL (July 2022), and 1347 mg/dL (January 2023). A comparison of the IV and SC doses showed that the patient's monthly IVIG dose (30 gm) was 25% less than the total monthly SCIG dose (40 gm).

Since the transition from SCIG to IVIG, the patient denies ADRs. Nursing assessments during monthly infusion visits noted that the patient's quality of life was improved after transitioning from SCIG to IVIG. The patient has remained stable on IVIG therapy since the transition. Patient preference was accommodated and resulted in improved patient satisfaction.

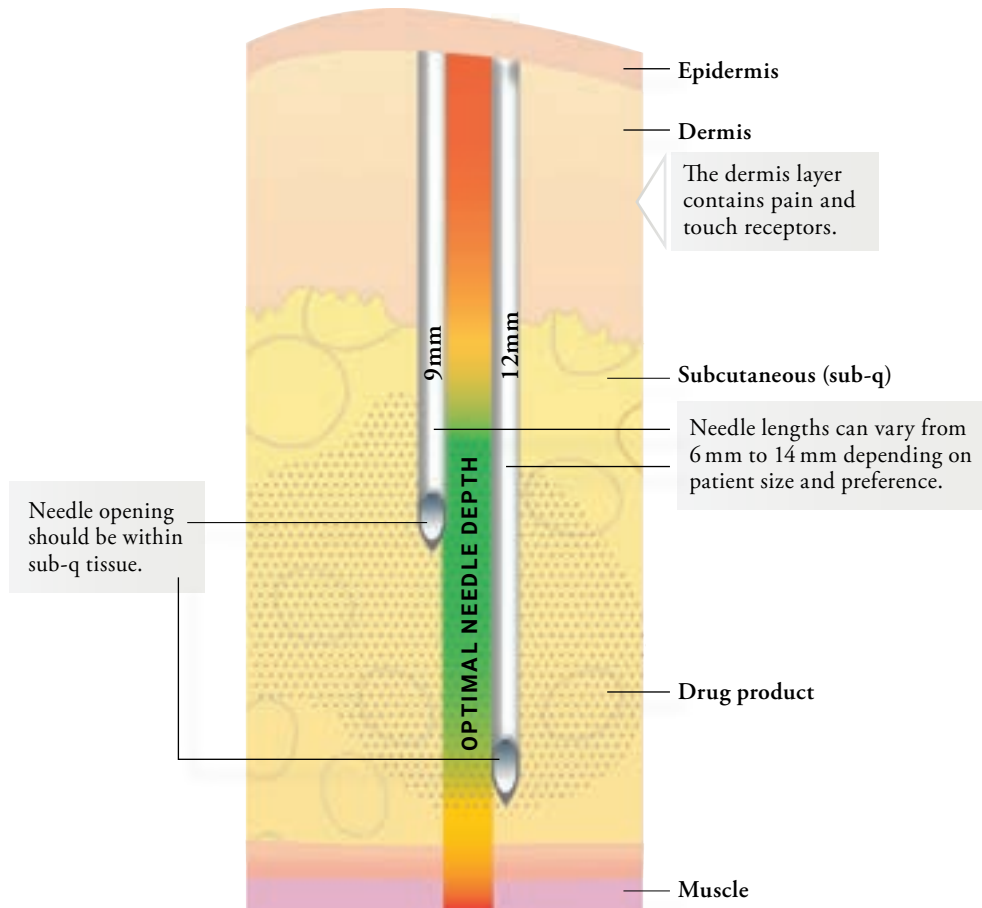
Discussion:

This case report supports the successful transition of a patient receiving a SCIG product back to an IVIG product. Successful transition was defined as adherence to infusions, management of ADRs, and response to treatment. This patient case report provides detail on a situation where the patient care is individualized on a continuous basis in conjunction with changes in the patient's clinical or personal situations.

A literature review identified an observational study that collected patient preference data using surveys with questions related to IVIG and SCIG variables including the route of administration (IV or SC), dosing frequency, site of care, number of needle sticks, and duration of infusions. According to the study, surveys of 252 patients reported that the site of care was the most essential attribute, and the route of administration was the least important of the attributes surveyed. Patients preferred the home for the site of care and shorter, less frequent infusions. Route of administration alone did not motivate patients to switch from IV to SC, and the site of care and shorter, less frequent infusions influenced patient preferences.¹

This patient case report highlights transitions between 2 routes of Ig infusions and the impact of the patient being an integral participant in the decision-making process. The start of care began with the patient receiving IV, followed by the transition to self administering SC, and then transitioned back to IV for quality-of-life preferences. The patient experienced ADRs with both administration methods. Initially, ADRs

FIGURE 1
Needle Placement for Subcutaneous Administration of Ig



from IVIG were treated with premedication, slowing the infusion rate and hydration. When administering SCIG, the pain and swelling were managed by slowing the infusion rate and adjusting the needle length to a longer needle. The longer needle length was necessary for proper placement in the deeper subcutaneous tissue and prevented infusion into the dermis (see Figure 1). The ADRs continued despite adjusting the needle lengths and ancillary supplies. The patient underwent ≥ 11 months of SCIG infusions before transitioning back to IVIG. The patient's CVID was managed effectively by treatment administered either IV or SC, and both options were available to the patient. Over the 7 years in this case report, the patient's specialty pharmacy

clinical team of nurses and pharmacists assisted the patient with changes to the treatment plan. They counseled the patient on the advantages and disadvantages of IV and SC administration and communicated regularly with the patient's prescriber. The professional services of pharmacists and nurses created seamless transitions between IV and SC.

Differences in IV and SC administration play a role in ADRs. Increased prevalence of systemic reactions was expected in IVIG and more local reactions in SCIG.² IVIG is generally administered in a single monthly dose, while SCIG is divided into weekly/bi-weekly infusions. The most common systemic ADRs for IVIG are headache and nausea. Many

IVIG ADRs are manageable with interventions such as slowing the rate of administration, oral or IV hydration, and providing medications for supportive treatment (antihistamines, antipyretics, or corticosteroids).³ The most common systemic ADRs for SCIG are similar to IVIG, but frequency and severity are generally less than IV. The most common ADR of SCIG is local infusion site reactions such as redness, itching, and swelling that can improve over time. This is unique to the SC route of administration and may lead a patient to transition from SC to IV.³

While IVIG or SCIG is a choice left to the discretion of each patient and their treating physician, several factors warrant consideration so that patients can make informed decisions that balance their needs, preferences, and lifestyles.³ According to a prospective observational study, 304 adult Ig patients were monitored over an

18-month duration of Ig treatment. Analysis of the individual health-related quality of life (HRQoL) measures revealed that differences in route and dosing schedules did not impact HRQoL in patients receiving Ig when treatment choice is shared by the patient and prescriber.⁴

The Immune Globulin Nursing Standards of Practice emphasize interdisciplinary aspects of patient care and include prescribers, pharmacists, and nurses.^{2,5} Successful treatment depends on expert clinical knowledge, experience, and a collaborative health care environment.² Clinicians and care providers can better serve patients when the decisions related to treatment variables of Ig largely remain a patient choice.

Conclusions

This patient case report highlights the importance of recognizing patient preference when choosing the route of administration for Ig therapy.

References

1. Mohamed AF, Kilambi V, Luo MP, Iyer RG, Li-Mcleod JM. Patient and parent preferences for immunoglobulin treatments: a conjoint analysis. *Journal of Medical Economics*. 2012;15(6):1183-91. doi: 10.3111/13696998.2012.716804.
2. IgNS Immunoglobulin Therapy Standards of Practice Committee. *Immunoglobulin Therapy: Standards of Practice*, 2nd Ed. Kirmse J, Schleis T, eds. Woodland Hills, CA: Immunoglobulin National Society; 2018.
3. Allen JA, Gelinis DF, Freimer M, Runken MC, Wolfe GI. Immunoglobulin administration for the treatment of CIDP: IVIG or SCIG? *Journal of the Neurological Sciences*. 2020;408:116497. doi: 10.1016/j.jns.2019.116497.
4. Pulvirenti F, Cinetto F, Pecoraro A, Carrabba M, Crescenzi L, Neri R, et al. Health-Related Quality of Life in Patients with CVID Under Different Schedules of Immunoglobulin Administration: Prospective Multicenter Study. *Journal of Clinical Immunology*. 2019;39(2):159-70.
5. Ness S. Differentiating characteristics and evaluating intravenous and subcutaneous immunoglobulin. *The American Journal of Managed Care*. 2019 Jun;25(6 Suppl):S98-S104. PMID: 31318515.



NHIA University offers one place to find education about every aspect related to home and alternate site infusion, with a searchable library of learning categories.

Revenue Cycle

Business & Leadership

Specialty Rx

Sterile Compounding

Nutrition Support

Immunoglobulin

RN Essentials

Anti-Infectives

Chemotherapy & other clinical topics



Online learning platform, free for all members



Earn and track CEs for:

- Pharmacists
- Pharmacy Techs
- Nurses
- Dieticians

-- NEW TO NHIA U --

NHIF Research Certificate Program (5 CE credits)

Learn the skills necessary to plan, conduct, and report original research.

NHIA members can log in with their member credentials. All staff at NHIA member organizations are eligible for access. If you need help enrolling additional staff members or with existing credentials, contact membership@nhia.org for support.

LEARN.NHIA.ORG

NHIA University is generously supported by **Baxter**



Baxter



HOME INFUSION

IT'S ALL ABOUT CARE

EVERYWHERE CARE IS GIVEN

When looking for a trusted partner to provide the needed products to help care for your patients, call your Baxter home infusion specialist. You'll have access to our broad portfolio of parenteral nutrition (PN) solutions, automated compounders, IV solutions, administration sets, IV pharmaceuticals, and more. With over 90 years of experience, and a broad portfolio of products to support your therapeutic needs, our dedicated home infusion sales team is ready to help.

We're where you need us.

It's easy. Call 1-888-229-0001 or visit www.baxter.com

- Automated Compounders and Parenteral Nutrition Solutions
- IV Solutions
- Administration Sets and Needle-free Connectors
- IV Pharmaceuticals