

Utilization and Tolerability of Alternative Infliximab and Biosimilar Dosing Strategies Among Adult Patients in the Home Infusion Setting: A Retrospective Study

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ABSTRACT

Introduction

Infliximab and its biosimilars are used to treat several chronic inflammatory conditions. While standard dosing is effective, patients can experience loss of response and require dose escalation, shortening dose intervals or higher doses.

Objective

To describe the use and tolerability of alternative infliximab dosing strategies in the home infusion setting.

Methods

This retrospective, multi-site observational study included adults (≥ 18 years) who received intravenous infliximab and its biosimilars infliximab-abda, infliximab-axxq, and infliximab-dyyb, over 2 years. Data on demographics, dosing, and adverse drug reactions (ADRs) were collected from the electronic medical records and analyzed descriptively.

Results

A total of 202 patients from 92 sites in the U.S. were included. Among those receiving alternative regimens, 22.8% received doubled dosing (10 mg/kg) and 8.9% received shortened intervals (every 4 weeks). ADRs occurred more often with the doubled dose group compared to shortened intervals (Difference 13.9%). Of patients who reported ADRs, 84.1% discontinued infliximab and 45% switched to another biologic. The most common ADRs reported were flushing, dyspnea, and chest discomfort, with 76.3% of ADRs managed in the home.

Conclusions

Alternative dosing strategies for dose escalation are utilized in the home infusion setting, but doubling the dose is associated with higher rates of reported ADRs compared to shortened intervals. These results highlight the importance of close monitoring and the need for future research to define optimal dosing approaches, balancing efficacy, safety, and practical challenges in home infusion care.

Keywords: Infliximab, biosimilar, home infusion, adverse drug reaction, dose escalation

Introduction

Infliximab, a tumor necrosis factor-alpha (TNF- α) inhibitor, is a medication for managing several chronic inflammatory conditions, including ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, and Crohn's disease.¹ Since the introduction of the reference product, Remicade[®] in 1998, several biosimilars have become available, offering more treatment options. Biosimilars reduce costs by introducing market competition, expanding patient access, and are approved as having comparable safety and efficacy to brand name medications. Providing infliximab in the home infusion setting is a convenient and cost-effective alternative to hospital-based infusions, improving patients' access to care and quality of life. The standard dosing regimen for infliximab is 5 mg/kg intravenously at 0, 2, and 6 weeks for induction, followed by maintenance infusions every 8 weeks.¹ While effective, a significant challenge in long-term infliximab therapy is the loss of response (LOR), with studies reporting that up to 46% of patients require dose escalation within the first year.^{2,3} This LOR can lead to increased health care costs (e.g., nursing allocation for more frequent home visits, ordering more drug for patients with higher prescribed doses), hospitalizations (e.g., infusion-related reactions and hypersensitivity that cannot be managed in the home), and a reduced quality of life (e.g., patients becoming symptomatic and do not maintain remission from their disease states), all of which have significant implications for home infusion providers managing these patients.

To overcome LOR, alternative dosing strategies such as shortened dosing intervals (e.g., every 4 weeks) or increased doses (e.g., 10 mg/kg) have been explored.⁴ These strategies aim to restore or maintain clinical response, but they also introduce complexities in home infusion management, including scheduling, drug preparation, monitoring for adverse events, and cost considerations. Potential disadvantages of alternative dosing strategies include the risk of serious infections and decreased quality of life due to more frequent infusions, which can be a burden for both patients and clinicians.^{1,5} Additionally, infliximab infusions can be associated with infusion reactions, both acute and delayed, which require careful management in the home setting.

Treatment is typically discontinued if there is no response by week 14 or if significant infusion reactions have occurred.¹ Acute infusion reactions

that are mild to moderate include pruritus, flushing, dyspnea, chest discomfort, hypertension, myalgia, nausea, urticaria, headache, skin rash, and dizziness during the infusion or within 1 to 2 hours of completion.⁷ More severe infusion reactions including bronchospasm, angioedema, hypotension, and related cardiovascular, cerebrovascular, and temporary vision loss have also been reported during and following infusion.⁸ Delayed infusion reactions, including serum-sickness-like reaction (SSLR) or maculopapular rash, can develop after more than 24 hours, or occur up to 1 to 3 weeks post infusion.⁹

This retrospective study aimed to evaluate the utilization and tolerability of alternative infliximab dosing strategies (shortened dosing intervals and increased doses) compared to standard dosing in the home infusion setting. By analyzing data from multiple home infusion sites, this research seeks to provide practical insights for clinicians to optimize infliximab therapy and improve patient outcomes. Specifically, the study focused on the infliximab reference product and its biosimilars.

Methods

This was a retrospective, non-randomized, multi-site observational study of infliximab utilization and tolerability in the home infusion setting. Patient data spanning 2 years were included in the analysis. This design allowed for the examination of prescribing practices and patient outcomes associated with infliximab therapy across various home infusion sites. The retrospective nature of the study utilized existing clinical data, allowing for the inclusion of a larger sample size. This study was determined to be exempt by the Institutional Review Board (IRB).

Patient Selection

Patients 18 years or older who had previously received or were actively receiving treatment with either the infliximab reference product (Remicade[®]) or its biosimilars Renflexis[®] (Infliximab-abda, REN), Avsola[®] (Infliximab-axxq, AVS), and Inflectra[®] (Infliximab-dyyb, IFX) at participating home infusion sites in the U.S. were included in the study. Patients were included if they received infliximab for any of its approved indications. Patients receiving subcutaneous Zymfentra[®] (infliximab-dyyb) were excluded from the study. This exclusion ensured that only patients receiving intravenous infliximab in the home infusion setting were analyzed.

Data Collection

Data was obtained through electronic medical records (EMR) from participating home infusion sites. The following data points were collected: baseline demographics, medication history, infliximab dosing strategy (standard or alternative), and adverse drug reactions. Dosing strategy was categorized as either standard (5 mg/kg intravenously at 0, 2, and 6 weeks for induction, followed by every 8 weeks for maintenance) or alternative (shortened dosing interval or increased dose). Dose escalation was defined as a dose increase or shortened interval. For patients in the dose increase group, the doubled dose population was assessed. Patients who had been switched between biologics for loss of response (LOR) or treatment failure were also recorded. LOR was measured by reported infusion reactions (acute, severe, and delayed), urgent medical intervention, or discontinuation of the biologic due to infusion symptoms. Shortened infusion durations of 1 hour, from the standard of 2-hour infusion, has been well studied to be safe and effective if a patient tolerated 4 standard sessions without infusion reactions.⁶ Whether a patient received a rapid infusion or standard infusion were not assessed in this study.

Data Analysis

Descriptive statistics were used to summarize patient demographics, dosing strategies, and adverse drug reaction rates. Categorical variables were presented as frequencies and percentages. For comparative analyses, differences in percentages between standard and alternative dosing strategies, as well as between infliximab products, were calculated and reported. Patient weights (kg) were rounded to the nearest whole number and doses were grouped to the nearest 100 mg per prescriber orders. Specifically, percent differences were used to compare the occurrence of adverse drug reactions and discontinuation rates across the different dosing groups and products.

Results

A total of 202 patients from 92 sites in the United States were included in this study. Baseline demographics of the patient population, including age and diagnoses, are presented in Table 1. The population was majority female and the frequency of infusions was variable. Other diagnoses included: hidradenitis suppurativa, lymphocytic colitis, posterior cyclitis, pyoderma gangrenosum, and sarcoidosis of lung. In this patient population, ages 18-27 (25.2%) had the most reported adverse drug reactions (Table 1). Figure 1 details the utilization of infliximab products and dosing strategies. Among patients receiving alternative dosing, 46 (22.8%) patients

TABLE 1 | Patient Characteristics (n=202)

	Patients (%)
Gender	
Male	79 (39.1)
Female	123 (60.9)
Age (range)	
18-27	51 (25.2)
28-37	35 (17.3)
38-47	41 (20.2)
48-57	44 (21.8)
58-67	22 (10.9)
68-77	9 (4.5)
Frequency of infusions	
Every 4 weeks	18 (8.9)
Every 5 weeks	2 (1)
Every 6 weeks	31 (15.3)
Every 8 weeks	151 (74.8)
Diagnosis	
Ankylosing spondylitis	4 (2)
Plaque psoriasis	8 (4)
Crohn's disease	107 (53)
Ulcerative colitis	56 (27.7)
Psoriatic arthritis	1 (0.5)
Rheumatoid arthritis	18 (8.8)
Other	8 (4)

FIGURE 1 | Doubled Dose vs. Shortened Internal, 2022-2024

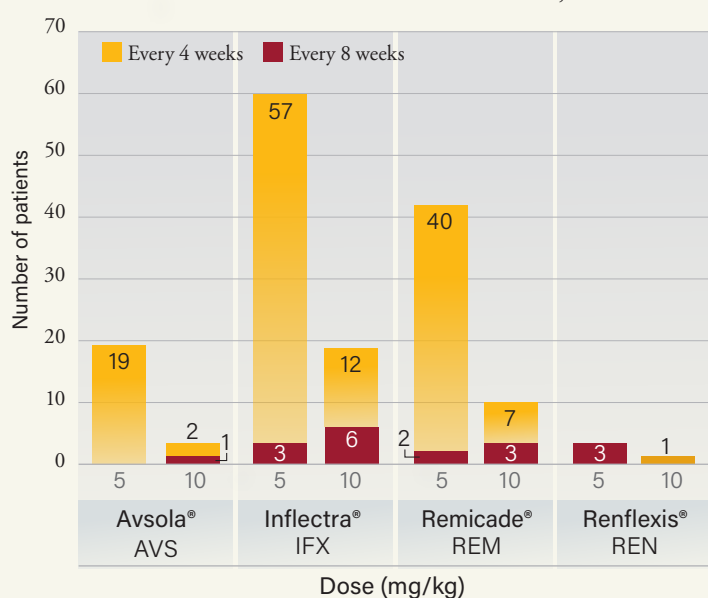


TABLE 2 | Reported Adverse Events (n=202)

	Patients (%)
Acute infusion reactions	
Abdominal pain	2 (1)
Chest discomfort	43 (21.2)
Diaphoresis	18 (9)
Diarrhea	3 (1.5)
Dizziness	17 (8.5)
Dyspnea	68 (33.7)
Flushing	79 (39.1)
Headache	15 (7.4)
Hypertension	4 (2)
Nausea	42 (20.8)
Pharyngitis	12 (5.9)
Pruritus	35 (17.3)
Rash	20 (10)
Tachycardia	9 (4.4)
Severe infusion reactions	
Anaphylaxis	2 (1)
Blurry vision	3 (1.5)
Coughing	17 (8.4)
Hives	16 (7.9)
Hypotension	6 (3)
Numbness	16 (7.9)
Rigors/chills	12 (5.9)
Seizure	1 (0.5)
Delayed infusion reactions	
Flu-like symptoms	2 (1)

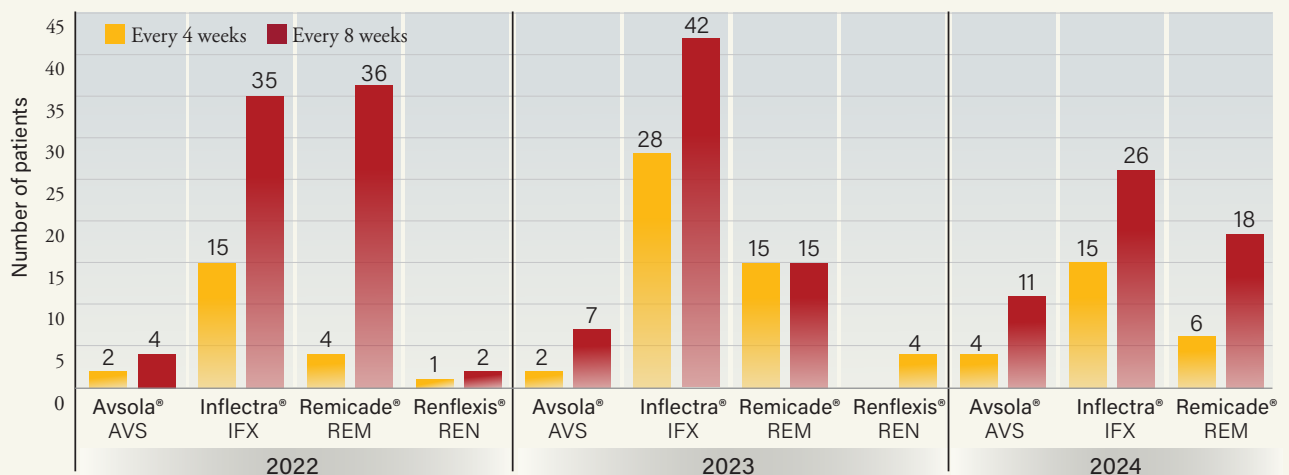
received double dosing of 10 mg/kg, and 18 (8.9%) patients received reduced frequency dosing every 4 weeks. IFX had both the highest percentage of patients experiencing adverse drug events in doubled dose 19 (9.4%) patients and shortened interval dosing 9 (4.4%) patients receiving 4-week dosing intervals. The doubled-dose population (10 mg/kg) compared to the shortened interval (every 4 weeks) had a difference of 13.9% adverse drug reactions reported. The difference in patients who had adverse drug reactions reported was higher in the increase dose population (7, 8, and 10 mg/kg) compared to the shortened interval (6, 5, 4 weeks) was 3.8%.

Tolerability of infliximab was assessed by evaluating the occurrence of adverse drug reactions and discontinuation rates. There were 170 (84.1%) patients who experienced an adverse drug reaction and discontinued infliximab, the 32 patients (15.8%) remaining continued the same therapy. Of the patients who discontinued treatment, 91 (45%) switched to a different biologic class. The most common adverse reactions were flushing, dyspnea, and chest discomfort (Table 2). Out of 224 reported adverse drug reactions 171 (76.3%) were managed in the home. The severity of adverse drug reactions was variable across the patient population as comorbidities were not individually assessed.

More-Frequent Administration Interval

An additional population of infliximab patients were assessed who did and did not experience adverse events. A total of 292 patients were included for frequency change from 8-week to 4-week intervals. From 2022 to 2023, IFX showed the highest percent increase (50%) of patients started on 8-week intervals and converted to 4-week intervals. Sixty percent of

FIGURE 2 | Total Patients With Infliximab Biosimilar Shortened Interval 4 weeks vs 8 weeks 2022-2024 (n = 292 patients)



total patients in the IFX group were on 4-week intervals in 2023, increasing to 63% of total patients in 2024. The REN group in 2023 had no patients on shortened interval dosing. In 2024, no patients were actively receiving REN. AVS had a gradual shift from 66% of total patients in 2022 to 73% in 2024 (Figure 2).

Discussion

This retrospective study evaluated the utilization and tolerability of alternative infliximab dosing strategies in the home infusion setting. The findings demonstrate that while alternative dosing strategies, including increased doses and shortened intervals, are utilized in this setting, there are important considerations regarding their tolerability. Specifically, a higher percentage of patients receiving increased infliximab doses experienced adverse drug reactions compared to those receiving shortened dosing intervals. This observation aligns with some previous research suggesting treatment success following dose escalation.^{4,5}

The increased incidence of adverse drug reactions with higher infliximab doses has several implications for home infusion practice.^{5,7} Close monitoring of patients receiving dose escalation is crucial to identify and manage potential adverse events promptly. This may require additional nursing time for patient education, follow-up phone calls, and coordination with the prescribing physician. Furthermore, pharmacies need to be prepared to handle dose adjustments and potential changes in infusion schedules. The financial impact of increased adverse events, including potential hospitalizations or the need for additional medications to manage side effects, should also be considered. Currently, pre-medications are optional for the patient but recommended by providers.

Shortened dosing intervals, while associated with a lower risk of adverse drug reactions in this study, also present challenges in the home infusion setting.⁵ More frequent infusions require more frequent scheduling, drug preparation, and delivery, which can strain resources and increase costs. Patient adherence may also be affected by the increased frequency of infusions, potentially leading to missed or delayed doses from scheduling difficulties. Unrelated to dosing, some patients discontinued an effective agent without any tolerability issues due to insurance coverage. The need to balance the potential benefits of shortened intervals in maintaining disease remission with the logistical and economic challenges in the home infusion setting is a critical consideration.

Study limitations were related to the retrospective, non-randomized design, where causality cannot be established, and there is a potential for bias in data collection and patient selection. Reported events occurred in the home or in an infusion center under the observation of a nurse. Premedication (corticosteroids, antihistamines, and/or antipyretics) was determined at the ordering provider's discretion, and the patient was given the option to decline prior to each infusion. It is unclear whether premedication was beneficial as this data could not be collected for all patients. A 2019 meta-analysis has found that corticosteroids and antihistamines were not associated with a reduced risk of infusion-related reactions in patients with immune-mediated inflammatory diseases.⁹ According to the Remicade® package insert, premedication is ordered at the provider's discretion.¹

Future research should explore the long-term effectiveness and cost of alternative infliximab dosing strategies in the home infusion setting. Prospective studies with a randomized controlled design are needed to confirm these findings and to identify optimal strategies for managing infliximab therapy in this population. Additionally, research focusing on patient-reported outcomes and quality of life would provide a more comprehensive understanding of the impact of different dosing strategies.

Conclusion

This study demonstrated the tolerability of the dose escalation group when adjusting for an increased tolerance of the medication. The severity of adverse drug reactions was variable across the patient population. However, the definitive reasoning for prescribing practices has yet to be determined. This analysis of dose increases and shortened intervals provides a baseline for prescribing patterns of infliximab biosimilars. Further studies are needed to provide background on prescriber initiation of therapy related to tolerability risk assessment for indications to determine what patients can receive dose escalation after therapy induction.

Disclosures

The authors have declared no potential conflicts of interest.

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