A Retrospective Cohort to Demonstrate the Impact of COVID-19 on Compliance Rates Among a Home Infusion Provider's Population of Multi-drug Resistant HIV-1 Infected Patients

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ABSTRACT

Background: The objective of this study was to demonstrate the impact of COVID-19 on compliance to ibalizumab-uiyk infusions, oral antiretroviral therapy (ART) regimen, and service discontinuation rate while using previously studied medication compliance strategies.[1] Experts agree, medication compliance is imperative to prevent transmission of drug-resistant HIV and further development of resistance to current treatment options.[2] A retrospective study conducted in 2019 showed 85% compliance to ibalizumab-uiyk and ART regimens in patients utilizing a compliance-focused care model.[1] However, a longitudinal study demonstrated a decrease in access to medications and increased cancellations of health care appointments during the COVID-19 pandemic.[3] Although literature is limited, results of previously published studies show a potential negative impact of COVID-19 on medication compliance among the HIV population.

Methods: This retrospective cohort analysis was conducted by evaluating a home infusion provider's electronic record of ibalizumab-uiyk-treated patients managed by a pharmacist-led, compliance-focused care model previously studied in 2019. Cohorts included patients receiving ibalizumab-uiyk during a pre-COVID-19 period (June 1, 2019 - February 28, 2020) and a post-COVID-19 period (April 1, 2020 - December 31, 2020). Outcome parameters included overall compliance rate of ibalizumab-uiyk, oral ART compliance rate, infusion site-of-care data, and service discontinuation rates.

Results: Overall ibalizumab-uiyk compliance rate between pre- and post-COVID-19 groups were 96% and 97%, respectively, showing no significant difference. Service discontinuation rates were observed at 23% (n=20) and 22% (n=19) between the pre- and post-COVID-19 groups, respectively, showing no significant difference. Oral ART regimen compliance was observed at 86% in the pre-COVID-19 group and 94% in the post-COVID-19 group showing a significant increase in the post-COVID-19 cohort. Site-of-care data showed that 85% of infusions were administered in the home setting for both groups.

Conclusion: Results show that utilization of a compliance-focused care model maintained compliance rates in ibalizumab-uiyk-treated patients during the COVID-19 public health emergency (PHE). More studies are recommended to demonstrate the impact of pharmacist-led compliance programs and how they can potentially avoid costly negative effects of non-compliance during a national pandemic.

Introduction

Over the last several decades there has been a significant increase in the use of antiretroviral therapies (ART) in the treatment of HIV. Newer ART agents have provided more effective options to reach viral suppression with a high barrier to resistance and lower side effect profile. However, drug resistance remains a concern for the HIV population. According to the World Health Organization (WHO) in 2019, an estimated 67% of people living with HIV globally receive ART treatment and 26% of people initiating treatment are infected with first-line ART drug resistant HIV.[2] In the United States, only an estimated 66% of HIV patients are virally suppressed which is concerning for the development of resistance.[4] The WHO warns that drug-resistant HIV jeopardizes the efficacy of ART treatment options and results in increased numbers of HIV infections and HIV-associated morbidity and mortality.[2]

Drug-resistant HIV can be transmitted from one infected person to another. This is considered pre-treatment HIV drug resistance. Drug resistance may develop post-treatment as well due to various causes such as poor medication compliance, inadequate absorption of ART, or initiating an ART regimen with a low barrier to resistance. Experts agree for both pre- and post-treatment HIV drug resistance, medication compliance is imperative to prevent transmission of drug-resistant HIV and further development of resistance to current treatment options. In addition, poor medication compliance is directly related to increased morbidity and mortality in HIV-infected patients.[5]

Several studies evaluated the reason for non-compliance specifically in the HIV population. One article states the most frequent reasons for non-compliance in HIV-infected patients included: the influence of dosing and formulations or "pill burden," ART-related adverse events, provider gap in up-to-date disease and treatment knowledge, poor provider-patient relationship, and lack of access to treatment.[5] In addition to identifying barriers, the article also cites results from several studies on approaches to overcome medication adherence barriers. These recommendations are supported by results of a study that showed increased adherence when a multidisciplinary approach was used.[5] In addition, continued patient education on HIV and open discussion on patient perceived barriers improved adherence. A study conducted by Hirsch et al., evaluated the impact of a pharmacist-managed medication therapy management (MTM) program on medication adherence among HIV/AIDS patients. The MTM program included counseling on adverse effects, evaluating barriers to adherence, and providing regimen recommendations to the provider. The results of the study showed consistently higher medication adherence rates in patients receiving MTM services at rates of 69.4% versus 47.3% in patients who did not receive MTM services.[6]

A retrospective study conducted in 2019 evaluated adherence rates in a home infusion provider's multidrug-resistant HIV-infected patients receiving ibalizumab-uyik infusions while implementing a pharmacist-managed clinical care model focused on compliance. Ibalizumab-uiyk is used in conjunction with oral antiretroviral therapy (ART), approved for individuals with multidrug-resistant HIV-1 who are failing their current ART therapy. The model included scheduled counseling for patients prior to each dispense to discuss medication compliance and adverse effects as well as to identify potential barriers to continued treatment. In addition, verification of oral ART compliance was confirmed with each ibalizumab-uiyk dispense. This model included providing updates and recommendations to the provider where clinically appropriate. The results of this study showed 85% adherence to ibalizumab-uiyk and oral ART regimen in patients utilizing a clinical care model focusing on compliance.[1]

During the COVID-19 pandemic period, studies showed a potential negative impact on adherence rates among the HIV population. A longitudinal study demonstrated a decrease in access to medications and increased cancellations of health care appointments during the COVID-19 pandemic.[2] One study demonstrated the negative impacts from the pandemic that resulted in lower medication adherence in an HIV population due to lack of access to medical services and medications. The results showed 22% of patients experienced at least one negative health consequence due to the impact of COVID-19.[7] Even though literature is limited, results of current published studies have concluded a negative impact on regimen adherence among HIV-infected patients during this period.

Although studies support the role of pharmacists in improving medication compliance and adherence in the HIV/AIDS population, studies are lacking to evaluate if pharmacists could maintain a significant role in positively impacting compliance during a public health emergency (PHE) such as the COVID-19 pandemic. Identifying results of

pharmacist-led compliance programs may be of benefit to support approaches to improving overall patient compliance, but also provide a solution to reduce the negative impact on compliance rates due to the reported lack of access to medical services and medications during a PHE.

Purpose

The objective of this study was to demonstrate the impact of COVID-19 on compliance to ibalizumab-uiyk infusions and oral ART regimen while using previously studied medication compliance strategies in a population diagnosed with multidrug-resistant HIV. Other objectives were to evaluate the impact of COVID-19 on service discontinuation rates and infusion site of care.

Methods

This was a retrospective cohort analysis of a national home infusion provider's ibalizumab-uiyk treated patients. Evaluated data included subjects' electronic record of ibalizumab-uiyk dispense history, oral ART compliance, service discontinuation, and infusion site of care. Cohorts were as follows: pre-COVID-19 patients receiving ibalizumab-uiyk infusions between June 1, 2019 and February 28, 2020 and post-COVID-19 patients receiving ibalizumab-uiyk between April 1, 2020 and December 31, 2020. It is difficult to specifically define the exact start date where COVID-19 restrictions impacted access to medications and medical care because restrictions and implementation dates varied by region. Because this study evaluated a national HIV population, March 2020 was excluded from both cohorts as a pre- and post-COVID transitional period to account for the variation.

Outcome parameters included overall compliance rate of ibalizumab-uiyk based on dispense history, oral ART compliance, service discontinuation rate, and infusion site of care. The electronic pharmacy dispense history of ibalizumab-uiyk for each patient treated between the study periods was evaluated based on receiving infusions at the time of the scheduled dose. Ibalizumab-uiyk infusions evaluated during the study were considered non-compliant if the maintenance dose was missed by more than 3 days based on ibalizumab-uiyk package insert dosing recommendation.[8] In the event a maintenance dose was missed by 3 or more days, a loading dose was provided before resuming maintenance dosing. Ibalizumab-uiyk compliance was calculated as total missed doses out of total infusions during the respective study period. Missed doses were further categorized as patient non-compliant or missed due to hospitalization or insurance delay where the pharmacist documented the reason for the missed maintenance dose. Patients were considered compliant if an ibalizumab-uiyk dose was missed due to hospitalization or insurance reasons. Additional outcomes included oral ART compliance and service discontinuation rate. Pharmacists verified oral ART compliance with each patient and with each patient's community pharmacy managing the oral ART regimen, prior to each ibalizumab-uiyk dispense.

Pharmacists were directed to document oral ART compliance in clinical assessments as part of the electronic patient record. Patients were considered compliant on oral ART regimen when documented as compliant in clinical assessments. Oral ART compliance rate was calculated by the overall average of individual patient compliance rates. Service discontinuation rates were evaluated in the pre- and post-COVID-19 cohorts to determine significant difference. Patients were considered discontinued from infusion services when documented as inactive within the patient electronic record. Site of infusion was compared between the 2 cohorts to evaluate if there was a significant change during the COVID-19 PHE. Patients included in the study had an option to receive their infusion either in an alternate site infusion center or in the home if the insurance provider allowed. All patients receiving ibalizumab-uiyk during the study periods were included in this study, there were no exclusions.

Results

Study patients are shown in Exhibit 1. The pre-COVID-19 cohort included evaluation of 87 patients and 1,000 infusions and the post-COVID-19 cohort included 88

EXHIBIT 1

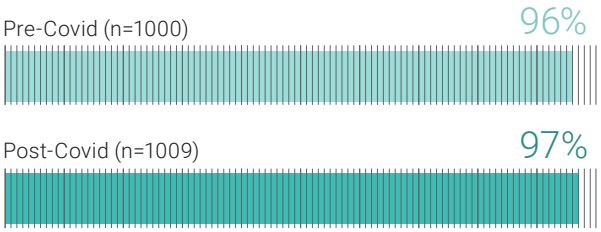
Inclusion Data

	Pre-COVID-19	Post-COVID-19
Total infusions (#)	1,000	1,009
Patients (#)	87	88
Gender	**Number (%)**	
Male	70 (80.5%)	69 (78.4%)
Female	17 (19.5%)	19 (21.6%)
Age	**Years (SD)**	
Median	56 (12.9)	56 (12.3)
Range	23-79	25-79

EXHIBIT 2

Ibalizumab-uiyk Infusion Compliance

P=0.287



patients and 1,009 infusions. There was no significant difference found between age and gender in the 2 cohorts. The median age for the pre- and post-COVID-19 group was 56 years with 80.5% male in the pre-COVID-19 group and 78.4% male in the post-COVID-19 group.

As shown in Exhibit 2, overall ibalizumab-uiyk compliance rates were observed at 96% in the pre-COVID-19 group and 97% in the post-COVID-19 group with no significant difference between cohorts (p=0.287). Further classification of missed doses showed that 38% (n=16) of missed doses in the pre-COVID-19 group and 31% (n=11) of missed doses in the post-COVID-19 group were due to patient non-compliance, resulting in no significant difference (p=0.165) [Exhibit 3].

The remaining missed doses in the 2 groups were classified as patient compliant due to unavoidable hospitalization or insurance delays. Service discontinuation rates were observed at 23% (n=20) for the pre-COVID-19 group and 22% (n=19) for the post-

EXHIBIT 3

Missed Ibalizumab-uiyk Infusions

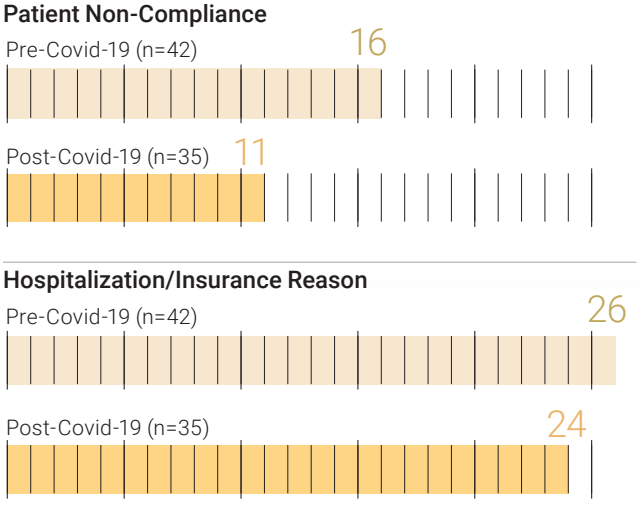


EXHIBIT 4

Service Discontinuation Rates

P=0.413

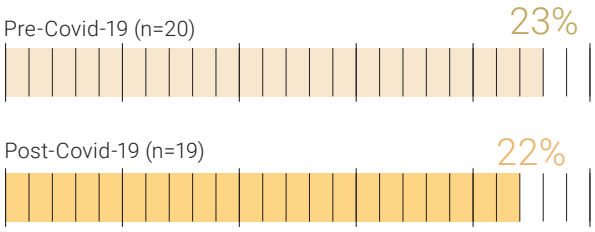
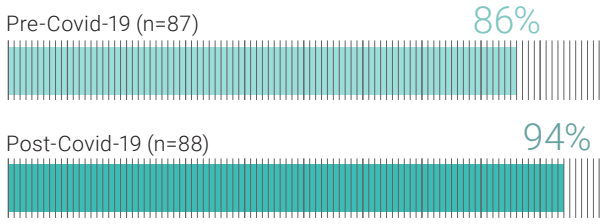


EXHIBIT 5

Oral ART Compliance

P<0.0001 (95% CI)



COVID-19 group (Exhibit 4). This resulted in no significant difference in service discontinuation rates between the 2 cohorts (p=0.413). Oral ART compliance rates for the pre-COVID-19 cohort were observed at an overall average of 86% where the post-COVID-19 cohort was observed at 94%, showing a significant increase in compliance in the post-COVID-19 cohort (p<0.0001) [Exhibit 5]. There was no difference observed in the site of care where 85% of ibalizumab-uiyk infusions were administered in the home for both groups.

Discussion

Pharmacist-led care models that focus on compliance have the potential to make a positive impact on patient medication compliance as demonstrated in this study. As a primary contact in the patient's HIV care, the pharmacist is a trusted health care professional who can counsel the patient to navigate known barriers to adherence shown in previously mentioned studies. Clinical pharmacists bring solutions by providing a multidisciplinary approach, managing side effects, providing continued patient education, and building patient-provider relationships. These key characteristics have been previously studied and demonstrated as important in preventing missed doses of critical medication in the HIV population. However, prior to this study, there was minimal published data showing the

impact that pharmacist-led compliance programs have on patient medication compliance during a PHE.

This study successfully demonstrated that the previously evaluated compliance-focused care model managed by pharmacists in patients treated with ibalizumab-uiyk, sustained compliance to ibalizumab-uiyk infusions as well as increased oral ART regimen compliance during the COVID-19 pandemic. Although it cannot be directly correlated, it is hypothesized that frequent pharmacist-patient interaction and patient follow-up with each infusion to evaluate for adverse effects and barriers to treatment had a positive impact leading to the results. This is consistent with previous study findings where pharmacist-led MTM programs have resulted in an increase in compliance rates.

Limitations include variations in electronic documentation for compliance to oral ART regimen. Although pharmacists were directed to document compliance in custom assessment templates for this patient population, there may be occurrences where compliance may have been documented by an alternate method such as a chart progress note which is not retrievable via reporting methods used in this study. In this research, patients were considered non-complaint if not documented in a custom assessment.

The results of this study prompted a broader evaluation of this multidrug-resistant HIV-infected population to increase the study period and number of patients evaluated. An extension of the original study, a retrospective evaluation of a national home infusion provider's approach to medication adherence of parenteral ibalizumab-uiyk conducted in 2019, was initiated after the result of this study found the positive outcomes with pharmacist-led care models. The extension of a previous retrospective study included all patients receiving ibalizumab-uiyk therapy serviced by an infusion provider since FDA approval in 2019 through March of 2021. This extension addressed the limitation of oral compliance documentation where all methods of documentation were evaluated for compliance. In addition, missed doses and service discontinuation were further categorized for reason of non-compliance to gain insight to the contributing factors to non-compliance. Results of the extension study were consistent with findings from the original study in 2019, where compliance to ibalizumab-uiyk infusions were maintained at 98% and oral ART regimen compliance was maintained at 89%. Service discontinuation evaluation observed 90% of the study population continued ibalizumab-uiyk infusions as expected or transitioned to alternate therapy.[9]

This study along with other published results demonstrate the positive impact of pharmacist-led care models on overall compliance in a population where medication compliance has been accepted as vital to reducing drug resistance, morbidity, and mortality. However, more studies are needed to demonstrate the importance of pharmacist-driven compliance programs during a PHE and whether these models can potentially avoid the costly negative effects of non-compliance. It is yet to be determined how the results from our study will be utilized, however it does support the use of this compliance-focused care model in this national home infusion provider's patient population.

Conclusion

During a public health emergency, studies have shown that access to medical services and medication are reduced, leading to a decrease in medication compliance. Utilizing pharmacist managed care models as part of a multidisciplinary team showed a positive impact on patient medication compliance in a multidrug resistant HIV-infected population.

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