Utilization and Tolerability of Crizanlizumab in the Home and Alternate Infusion Settings

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Background

Sickle cell disease (SCD) is an inheritable hemoglobinopathy that affects an estimated 100,000 people in the United States of America.[1] Vaso-occlusive crises (VOCs) are a hallmark of sickle cell disease that often results in hospitalizations and can result in organ damage and complications such as acute chest syndrome, splenic sequestration crisis, venous thromboembolism, and priapism.[2] The major clinical manifestation of VOCs are acute painful crises. Over three-fourths of SCD-related hospitalizations in 2016 involved a pain crisis.[3] The number of hospital admissions for sickle cell pain crises increased from 2016 through 2020.[4] Several new therapies have come to market in recent years to prevent the sickling of red blood cells, reduce VOCs, correct mutations in the gene encoding hemoglobin A, or induce expression of fetal hemoglobin.

Crizanlizumab was FDA approved in 2019 to reduce frequency of VOCs in patients with SCD. Crizanlizumab is a humanized monoclonal antibody that inhibits P-selectin activity that works by binding to activated P-selectin on the surface of endothelial cells and platelets.[5,6] This binding facilitates the inhibition of platelets, red blood cells, and leukocytes interactions thereby resulting in decreased platelet aggregation, increased blood flow and decreased vaso-occlusion.

Despite extensive healthcare needs, many patients with SCD have difficulty accessing appropriate care.[1] Home infusion provides a level of convenience and can minimize geographic barriers to accessing treatment. While crizanlizumab has been shown to significantly reduce the rate of sickle cell related pain crises with a low incidence of adverse events[5], limited data exists pertaining to the usage and tolerability of crizanlizumab in home and alternate infusion site settings.

Purpose

This research provides evidence of the clinical utility and positive impact on patient access to SCD treatment in home and alternate infusion site setting. The primary objective of this study was to assess usage of crizanlizumab in home and alternate infusion site patients. A secondary objective of this research was to assess patient tolerability of crizanlizumab in this patient population.

Methods

This retrospective, multi-center chart review evaluates 52 months of data on patients receiving crizanlizumab. Baseline characteristics, demographics, and adverse drug reactions will be reviewed. This study was determined to be exempt by the IRB.

Patients aged 18 and older with a confirmed diagnosis of sickle cell disease and at least one dispense of crizanlizumab (since its FDA approval) were included. The following data, if available, was also reviewed:

- Number of patients that discontinued therapy (and reason)
- Frequency and types of ADEs
- Adherence to FDA approved labeling (dose and schedule)
- Missed Doses
- Payer Type
- Characteristics of referral sources (physician specialty, local disease burden)
- Site of administration (home or alternate infusion setting)
- Use of other medications approved for SCD
- Frequency of VOC-related hospitalizations

Disclosures

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation: Kascha Brown; Maria Giannakos; Christopher Roy; Annemarie Hocking: Nothing to disclose.

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Figure 1: Crizanlizumab Infusion Setting

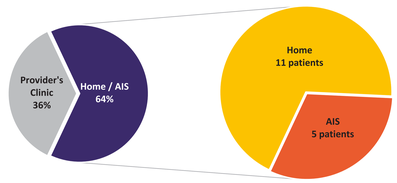

Figure 2: Medication Aderence Dispense Ratio

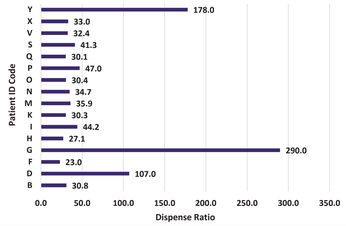

Figure 3a: United States Geographic Regions

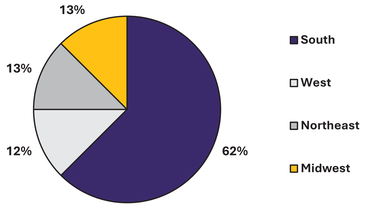

Figure 3b: Geographic Distribution of Patients

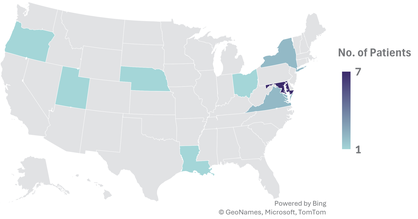

Figure 4: Reasons for Crizanlizumab Discontinuation

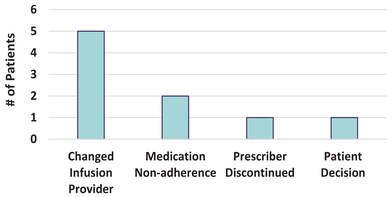

Table 1: Patient Characteristics (n=16)

Age at First Dispense	
Mean (SD), years	27.81 (7.32)
Median, years	25.5
Age Groups, # Patients (%)	
18-24	7 (43.75)
25-34	7 (43.75)
35-44	1 (6.3)
45-54	1 (6.3)
Sex, # (%)	
Male	11 (68.8)
Female	5 (31.2)
Sickle Cell Genotype, # (%)	
HbSS	11 (68.8)
HbSC	2 (12.5)
Not reported	3 (18.7)
Payer Type, # (%)	
Commercial Insurance	10 (62.5)
Medicaid	6 (37.5)
Prescriber Specialty, # (%)	
Hematologist / Oncologist	14 (87.5)
Primary Care (Family Medicine, Internal Medicine)	2 (12.5)
Patients with Reported Concurrent Medications, # (%)	
Hydroxyurea	13 (81.3)
Voxelotor	4 (25)
L-glutamine	1 (6.3)
Folic Acid	9 (56.3)
Patients with Reported Hospitalizations, # (%)	8 (50)

Results

This study evaluated the utilization and tolerability of crizanlizumab in 25 patients with sickle cell disease (SCD) across various infusion settings. Of these, 9 patients (36%) received their infusions in a provider clinic setting, while the remaining 16 patients (64%) received their infusions at home or in an alternate infusion site (AIS). Among the 16 patients treated outside of a clinic, 11(69%) received crizanlizumab at home, and 5 (31%) were treated in an AIS *(Figure 1)*.

The patient sample consisted of 17 males (68.8%) and 8 females (31.2%), with an average age of 27.81 years (± 7.32) and a median age of 25.5 years at the first dispense *(Table 1)*. Most patients were in the 18–34-year age range, with 7 patients (43.75%) aged 18–24 years and another 7 patients (43.75%) aged 25–34 years. Regarding payer types, 10 patients (62.5%) had commercial insurance, and 6 patients (37.5%) were covered by Medicaid. The predominant genotype amongst patients included in this study was HbSS (68.8%) whereas only 12.5% of patients presented with the HbSC genotype.

Patients were on service for pharmacy services for an average of 416 days and a median of 343 days, indicating a positive skewed distribution. This might be attributed to the high discontinuation rate observed in the dataset. A dispense ratio was calculated in order to better quantify medication adherence *(Figure 2)*. The number of days on service was divided by the number for dispenses. This ratio was calculated for each patient. The data of three patients can be perceived as outliers since their dispense ratios were 107, 178, and 290. Interestingly, two of these patients were discharged for non-compliance and the third switched infusion providers due to issues with insurance authorizations. The outliers skew the dispense ratio to 63. Omitting the outliers reveals a mean ratio of 33.85 (SD 6.7) and a median of 32.44, values more in line with the FDA approved dosing schedule of once every 28 days.

Geographically, the 16 patients receiving home or AIS treatments were distributed throughout the United States as follows: 10 patients (62.5%) were from the South region, 2 patients (12.5%) from the West region, and 2 patients (12.5%) from the Midwest region and 2 patients were from the Northeast region *(Figures 3a & 3b)*. Of the 16 patients treated outside a clinic, 9 (56.3%) discontinued therapy during the study period. The reasons for discontinuation were varied: 2 patients (12.5%) discontinued due to medication nonadherence, 5 patients (31.3%) switched to another infusion provider, 1 patient (6.3%) discontinued at their own choice, and 1 patient (6.3%) discontinued based on the provider's discretion *(Figure 4)*.

In terms of co-treatment for Sickle Cell Disease, most patients were taking additional therapies alongside crizanlizumab *(Table 1)*. Hydroxyurea was the most commonly co-prescribed medication, with 13 patients (81.3%) receiving it. Patients were also co-treated with folic acid (56.3%), voxelotor (25%), and L-glutamine (6.3%). Notably, no adverse drug reactions (ADRs) or use of anaphylaxis kits were reported during the study. The study also found that eight patients (50%) had reported hospitalizations due to sickle cell crises during the study period.

Discussion

This study aimed to evaluate the clinical utility of crizanlizumab in home and alternate infusion settings for patients with sickle cell disease. The findings suggest that crizanlizumab can be effectively utilized outside traditional clinic settings, with a substantial proportion of patients (64%) receiving their infusions at home or in alternative infusion suites. However, the results also reveal a relatively high discontinuation rate, with 56.3% of patients in the home or alternate settings discontinuing therapy during the study period. Notably, five of these nine patients switched to a different infusion provider (Figure 4). Two of the remaining four patients were discontinued due to medication nonadherence. One patient discontinued therapy at the prescriber's discretion.

The findings are consistent with previous studies that have explored factors contributing to the discontinuation of crizanlizumab. Nonadherence to scheduled infusion appointments was a significant reason for discontinuation in a previous report5, a factor that was also evident in this study where two patients discontinued due to medication nonadherence. A perceived lack of efficacy has also been reported as a reason for discontinuation[7] and was also identified as a factor for some patients in this cohort. Each of the 8 patients receiving infusions in non-clinic settings that reported hospitalizations were co-prescribed hydroxyurea. Two patients were co-prescribed voxelotor, one patient was prescribed L-glutamine, and five patients were co-prescribed folic acid.

These factors highlight the ongoing challenges in maintaining adherence to crizanlizumab therapy, which may require further investigation into the reasons behind patients' choices to discontinue treatment, miss appointments, or switch providers.

This study's retrospective nature and small sample size are significant limitations. A broader, prospective study would provide more robust data, particularly concerning the reasons for discontinuation and the long-term effectiveness of crizanlizumab in home and alternate settings. Furthermore, variations in state-specific regulations and different pharmacy practices complicate the interpretation of results, as demonstrated by the incomplete data for some patients.

Nevertheless, the study provides valuable insights into the utilization of crizanlizumab in real-world settings and underscores the potential benefits of expanding access to infusion therapy outside the clinic.

Conclusions

This study demonstrates that crizanlizumab can be utilized in home and alternate infusion settings for patients with sickle cell disease. However, the high discontinuation rate highlights the need for further research to identify barriers to treatment adherence and optimize care delivery in non-traditional settings. These findings contribute to the growing body of evidence supporting the use of home infusion therapies for chronic conditions like sickle cell disease, offering a potential model for improving patient access to care. Future studies with larger sample sizes and a prospective design are needed to confirm these findings and explore strategies to improve patient adherence and long-term outcomes.

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