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Real-World Crizanlizumab Treatment Patterns of Patients with Sickle Cell Disease

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KEY FINDINGS & CONCLUSIONS

- This real-world evidence suggests that 66% of patients who receive crizanlizumab receive ≥4 doses within 6-months.
- There was a reduction in mean gap days after the first dose. Median gap days demonstrated that most of these patients received each dose on schedule.
- Of those who discontinued treatment, 31% restarted crizanlizumab within 6-months post-index.
- Future research investigating reasons for discontinuation or gaps between doses is warranted.

INTRODUCTION

Background

- Sickle cell disease (SCD) is an inherited blood disorder. It is characterized by vaso-occlusion and results in vaso-occlusive crises (VOCs) and progressive systemic manifestations.[1,2]
- SCD treatment options have been limited historically. Blood transfusions and pain management served as the mainstays of care until 1998 when the antineoplastic agent hydroxyurea (Droxia®) became the first FDA-approved drug for the treatment of SCD.[3] It remained the only approved pharmacological SCD treatment option until 2017 with the approval of L-glutamine (Endari™), followed in November of 2019 by crizanlizumab (Adakveo®) and voxelotor (Oxbryta™).
- Crizanlizumab (ADAKVEO®) is a humanized monoclonal antibody indicated to reduce the frequency of VOCs in patients ≥ 16 years of age with SCD.[4]
- Given its recent approval, published evidence on the real-world use of crizanlizumab is limited.

METHODS

Study Design

- Retrospective descriptive analysis using IQVIA's US-based Longitudinal Patient-Centric Pharmacy and Medical Claims databases. See study schematic (**Figure 1**).
- These are open-source administrative claims data, with pharmacy claims collected directly from retail, mail, long-term care, and specialty pharmacies and medical claims derived from the CMS-1500 billing form. Medical claims are largely outpatient in nature.

Objective

- To describe the real-world treatment patterns of crizanlizumab in patients with SCD initiating crizanlizumab in the U.S.

Outcomes

Crizanlizumab doses administered; gap-days between crizanlizumab doses; crizanlizumab discontinuation (≥60-day gap); days on crizanlizumab prior to discontinuation; crizanlizumab restarts.

Patient Selection

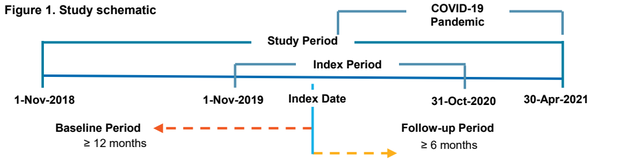
Inclusion Criteria
- ≥ 1 claim with SCD diagnosis within the study period.
- ≥ 1 claim for crizanlizumab within the index period, the first crizanlizumab claim is the index date.
- ≥ 16 years of age on the index date.
- Linkage between the Longitudinal Patient-Centric Pharmacy and Medical Claims databases within the study period.
- Data stability and patient eligibility during the 12 months prior to the index date.
- Data stability and patient eligibility during the 6 months following the index date.

Statistical Analysis

- This was a descriptive study and involved no comparative analyses.
- Days supply was set to 14 days for the initial crizanlizumab dose and 28 days for each subsequent dose, per the label-recommended dosing schedule.
- Gap days between crizanlizumab doses was calculated among patients that did not discontinue crizanlizumab during the 6-months post-index as the days between end of days supply of one dose to the next administration.
- Discontinuation was defined by a ≥60 gap days between doses, or ≥60 days from the end of days supply to the end of follow-up.
- Restart was defined as a crizanlizumab dose received after discontinuation.

RESULTS

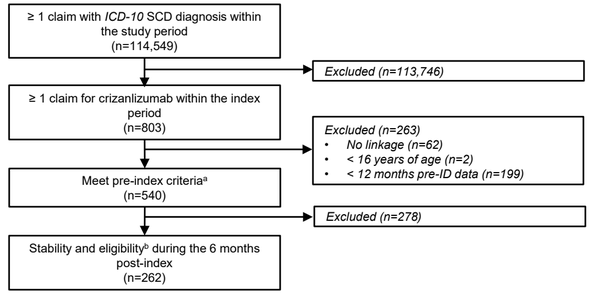
Figure 1. Study schematic



Attrition of the Study Sample

- A total of 262 SCD patients with crizanlizumab initiation met the study criteria (**Figure 2**).

Figure 2. Attrition of the study sample



ICD-10= International Classification of Diseases, Tenth Revision; SCD= sickle cell disease
[a] Linkage between the pharmacy and medical claims databases; at least 16 years of age; at least 12 months of pre-index data
[b] Stability (consistent reporting from pharmacies and providers during specified period) and eligibility (claim observed in specified period) in both the pharmacy and medical claims databases.

Patient Characteristics

- The majority (62%) were female;
- Most (53%) were in the 16- to 34-year age group;
- The southern geographic region had the highest representation (63%);
- Many had commercial insurance (47%), followed by Medicaid insurance (28%) and Medicare insurance (24%);
- As a measure of baseline comorbidities, 42% of patients had a Charlson comorbidity index of 0, meaning no comorbidities were found.
- Most (60%) had hydroxyurea use observed in the 12-months pre-index.

Table 1. Baseline patient demographics

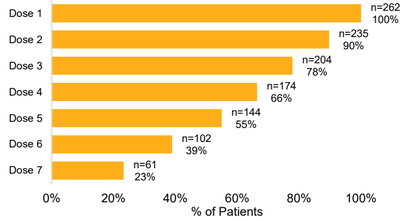
Total (n, %)	262	100%
Age Group (years) (n, %)		
16-17	1	0.38 %
18+	261	99.62 %
16-34	140	53.44 %
35-54	96	36.64 %
55+	26	9.92 %
Sex (n,%)		
Male	99	37.79 %
Female	163	62.21 %
Geographic Region (n,%)		
Northeast	27	10.31 %
Midwest	34	12.98 %
South	164	62.60 %
West	37	14.12 %
Insurance type on index claim (n,%)[1]		
Commercial	123	46.95 %
Medicaid	74	28.24 %
Medicare	64	24.43 %
Unknown Insurance	1	0.38 %
Charlson comorbidity index (CCI)		
0	111	42.37 %
1	63	24.05 %
2+	88	33.59 %
History of SCD treatment, 12 months pre-index (n, %)[2]		
Pre-index use of hydroxyurea	156	59.54 %
Pre-index use of L-glutamine	37	14.12 %
Pre-index use of voxelotor	2	0.76 %

[1] When multiple payer types were observed, the following hierarchy was used: Medicare, Commercial, Medicaid, Cash, Unspecified. When commercially-managed Medicaid was observed, the Medicaid designation was assigned.
[2] For the data sources used in this study, data for voxelotor appeared at least in part to be blocked by the manufacturer

Proportion of Patients Receiving Crizanlizumab Doses

- Of these patients, 235 (90%) received dose #2, 204 (78%) received dose #3, and 174 (66%) received ≥4 doses (**Figure 3**).

Figure 3. Proportion of patients (%) receiving each dose, in the 6-months post-index



Adherence among Patients Receiving Crizanlizumab

- Among the 112 patients that did not discontinue crizanlizumab in the 6-months post-index, the mean (standard deviation [SD]) and median (interquartile range [IQR]) gap days can be seen in (**Table 2**).
- Within the 6-months post-index, 150 (57%) of patients that initiated crizanlizumab discontinued crizanlizumab.
- Median (IQR) of 125 (43-180) days on therapy prior to discontinuation.
- Of those patients who discontinued crizanlizumab, 46 (31%) restarted crizanlizumab.
- At the end of the 6-months of follow-up, 88 patients (34% of all patients) appeared to be on crizanlizumab.

Table 2. Number of gap days between doses, among patients that did not discontinue crizanlizumab in the 6-months post-index

Number of gap days between dose 1 and dose 2		
Valid n, %	112	42.75%
Mean, SD	7	8
Median, (Q1-Q3)	1	(1-15)
Number of gap days between dose 2 and dose 3		
Valid n, %	112	42.75%
Mean, SD	4	6
Median, (Q1-Q3)	1	(1-6)
Number of gap days between dose 3 and dose 4		
Valid n, %	112	42.75%
Mean, SD	4	7
Median, (Q1-Q3)	1	(1-3)
Number of gap days between dose 4 and dose 5		
Valid n, %	112	42.75%
Mean, SD	5	7
Median, (Q1-Q3)	1	(1-7)
Number of gap days between dose 5 and dose 6		
Valid n, %	99	37.79%
Mean, SD	4	7
Median, (Q1-Q3)	1	(1-4)
Number of gap days between dose 6 and dose 7		
Valid n, %	61	23.28%
Mean, SD	2	3
Median, (Q1-Q3)	1	(1-1)

Limitations

- This study had several limitations, including those inherent to the use of claims: a prescription claim indicates only that a prescription has been filled, not if the prescription has been taken; diagnoses may be miscoded due to either operator error, or as a result of nuances in insurance coverage; care that occurs outside of the systems and providers reporting to the data source may not be captured; as the medical claims database is primarily generated in the process of outpatient encounters, resource utilization or certain events may be under-reported (e.g., inpatient encounters); nuances of patient care that are not included on insurance claims such as reasons for discontinuation are not available.
- Open-source databases pose additional limitations compared to traditional closed source claims databases including a lack an enrollment file to assess continuous enrollment. A proxy measure that relied on health service utilization was used to determine continuous activity instead.
- For the data sources used in this study, data for voxelotor appeared at least in part to be blocked by the manufacturer.
- The impact of COVID-19 restrictions or other access barriers to crizanlizumab use were not able to be assessed with this data.

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Disclosures

This work was funded by Novartis. Jincy Paulose, Soyon Lee, and Glorian Yen are employees of Novartis. Marie Yasuda, Chi-Chang Chen, Catherine McGuiness, and Jing He are employees of IQVIA, which was contracted by Novartis to perform this study.

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(1) Shah, N., Bhor, M., Xie, L., Paulose, J., Yuce, H., 2019. Sickle cell disease complications: Prevalence and resource utilization. PLOS ONE 14, e0214355. (2) Sundd, P., Gladwin, M.T., Novelli, E.M., 2019. Pathophysiology of Sickle Cell Disease. Annu Rev Pathol 14, 263–292. (3) U.S. Food & Drug Administration, 2020. The FDA Encourages New Treatments for Sickle Cell Disease. FDA. (4) Adakveo®. Package Insert., 2019.