Patient Demographic and Clinical Characteristics Associated with the Use of the Newly approved Disease-Modifying Medications for Sickle Cell Disease

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INTRODUCTION

Sickle cell disease (SCD) is a rare, inherited monogenetic blood disorder that disproportionately affects Blacks and African Americans (<90%).[1]

- Approximately 100,000 individuals in the United States are estimated to be affected by SCD.[1]

- Sickle cell disease patients may experience a series of acute (e.g., Vaso-occlusive crisis [VOC]) and chronic complications, which results in high healthcare resource utilization.

- The estimated total economic burden of SCD in the US was $2.98 billion (adjusted to 2015 US dollar) per year.[3]

Disease-modifying Treatments (DMTs): target key components of the SCD pathophysiological processes, and can efficiently prevent, mitigate, and ameliorate SCD complications.

- Hydroxyurea was the only DMT for SCD approved by the FDA for over 20 years.

- Data on real-world use of newly approved DMTs are limited.

Drug	Eligible age	Approval date	Mechanism of action[4]
L-glutamine	>=5 years	07/07/2017	Increase NADPH and reduce reactive oxygen species
Crizanlizumab	>=16 years	11/15/2019	Anti-P-selectin monoclonal antibody with reduction in red cell adhesion
Voxelotor	>=12 years >=4 years	11/25/2019 12/17/2021	Increase HbS oxygen affinity with reduced hemolysis

Objective: This study aimed to identify demographic and clinical characteristics associated with the utilization of the newly approved DMTs.
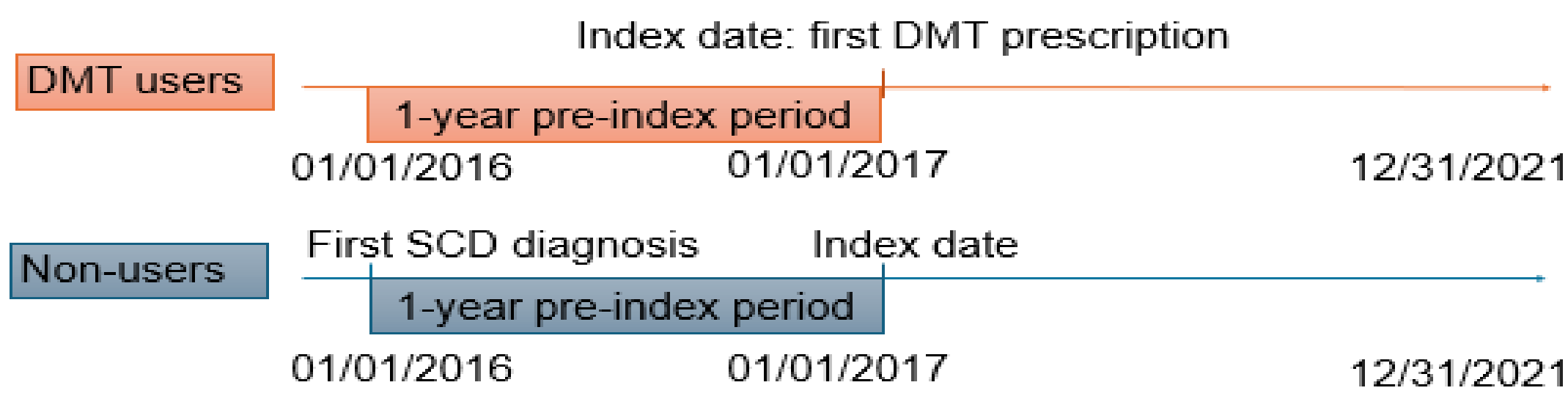
METHOD

➢ **Study design**
- Retrospective, longitudinal cohort study

➢ **Data source**
- 2016-2021 Merative™ MarketScan Commercial Database

➢ **Inclusion criteria**
- Patients had ≥1 inpatient or ≥2 outpatient visits with an SCD ICD-10 diagnosis code on separate dates between 01/01/2016-12/31/2021.
- Age between 5-64 years old at the index date.
- Continuously enrolled for 1 year before the index date.

METHOD

➢ **Exclusion criteria**
- Patients without pharmacy coverage were excluded.
- Patients with a cancer diagnosis were excluded.

➢ **Index date**
- DMT users: the date of the first prescription filled
- Non-users: 1 year after the first SCD diagnosis during the study period

Index date: first DMT prescription
DMT users
1-year pre-index period
01/01/2016   01/01/2017   12/31/2021

Non-users   First SCD diagnosis   Index date
1-year pre-index period
01/01/2016   01/01/2017   12/31/2021

➢ **Demographic characteristics:** Age, sex, region, metropolitan statistical area

➢ **Clinical characteristics:** The number of SCD-related outpatient visits, the number of VOC episodes, and the use of hydroxyurea within the 1-year pre-index period

➢ **Statistical analysis:** descriptive analysis and multivariate logistic regression.

RESULTS

➢ **Patient characteristics**

	Overall	Non-user	Any type	p-value[1]	L-glutamine	Crizanlizumab	Voxelotor	p-value[2]
n	5138	4,853	285		128	53	132	
Mean age (std)[a]	30.1(16.1)	30.2(16.1)	28.8(14.6)	0.2204	25.8(14.4)	32.1(10.6)	31.3(15.5)	0.0008
Age group[a]								
5-12	848(16.5%)	816(16.8%)	32(11.23%)		28(21.9%)	0(0%)	4(3.0%)	
13-17	535(10.4%)	487(10.0%)	48(16.8%)		21(16.4%)	4(7.6%)	29(22.0%)	
18-26	991(19.3%)	928(19.1%)	63(22.1%)		23(18.0%)	14(26.4%)	31(23.5%)	
27-34	748(14.6%)	701(14.1%)	47(16.5%)	0.2181	18(14.1%)	14(26.4%)	17(12.9%)	0.0009
35-44	869(16.9%)	824(17.0%)	45(15.8%)		23(18.0%)	13(24.5%)	17(12.9%)	
45-55	698(13.6%)	667(13.7%)	31(10.9%)		10(7.8%)	8(15.1%)	20(15.2%)	
56-64	449(8.7%)	430(8.9%)	19(6.7%)		3(3.9%)	0(0%)	14(10.6%)	
Sex[b]								
Male	2177(42.4%)	2,061(42.5%)	116(40.7%)	0.5574	51(39.8%)	25(47.2%)	50(37.9%)	0.5034
Female	2961(57.6%)	2,792(57.5%)	169(59.3%)		77(60.2%)	28(52.8%)	82(62.1%)	
Region[b]								
Northeast	907(17.7%)	857(17.7%)	50(17.5%)		27(21.1%)	8(15.1%)	24(18.2%)	
Northcentral	725(14.1%)	694(14.3%)	31(10.9%)	0.2854	14(10.9%)	9(17.0%)	10(7.6%)	0.3387
South	3258(63.4%)	3,072(63.3%)	186(65.3%)		76(59.4%)	33(62.3%)	92(69.7%)	
West	248(4.8%)	230(4.7%)	18(6.3%)		11(8.6%)	3(5.7%)	6(4.6%)	
MSA area[3,b]								
Non-MSA	296(5.8%)	278(5.7%)	18(6.3%)		2(1.6%)	3(5.7%)	13(9.9%)	
MSA	4232(82.4%)	4,020(82.8%)	212(74.4%)	0.0003	104(81.3%)	45(84.9%)	85(64.4%)	0.0021
Unknown	610(11.9%)	555(11.4%)	55(19.3%)		22(17.2%)	5(9.4%)	34(25.8%)	
Hydroxyurea use[b]								
No	3778(73.5%)	3,665(75.5%)	113(39.7%)	<.0001	52.2(42.2%)	23(43.4%)	49(37.1%)	0.6203
Yes	1360(26.5%)	1,188(24.5%)	172(60.4%)		74(57.8%)	30(56.6%)	83(62.9%)	
Mean number of VOC episodes (std)[a]	3.7(3.9)	1.9(3.2)	5.0(5.5)	<.0001	4.6(4.7)	9.9(6.9)	4.4(5.3)	<.0001
Number of SCD-related outpatient visits[a]								
<=4	2054(40.0%)	2,025(41.7%)	29(10.2%)		19(14.8%)	2(3.8%)	9(6.8%)	
5-9	1671(32.5%)	1,575(32.5%)	96(33.7%)	<.0001	41(32.0%)	9(17.0%)	52(39.4%)	0.0023
>=10	1413(27.5%)	1,253(25.8%)	160(56.1%)		68(53.1%)	42(79.3%)	71(53.8%)	

[1]Bivariate comparisons between DMT users and non-users; [2]Bivariate comparisons between specific types of DMT users; [3]Metropolitan statistical area
[a] Wilcoxon-Mann Whitney test or Kruskal Wallis test; [b] Chi-square test

➢ **Logistic regression**

Patient characteristics	Odds Ratio	95% CI	p-value
Age group (ref: 5-12)			
13-17	2.33	(1.44-3.75)	0.0005
18-26	1.29	(0.82-2.04)	0.2697
27-34	1.34	(0.83-2.18)	0.2346
35-44	1.22	(0.75-1.98)	0.4168
45-55	1.22	(0.72-2.06)	0.4676
56-64	1.21	(0.66-2.22)	0.5401
Sex (ref: Male)			
Female	1.19	(0.92-1.54)	0.1878
Region (ref: Northeast)			
Northcentral	0.8	(0.49-1.28)	0.3432
South	0.92	(0.66-1.29)	0.6326
West	1.33	(0.75-2.39)	0.333
MSA area (ref: MSA)			
Non-MSA	1.22	(0.72-2.07)	0.4665
Unknown	2.1	(1.47-2.86)	<.0001
Hydroxyurea use (ref: no)			
Yes	2.85	(2.19-3.72)	<.0001
Mean number of VOC episodes	1.1	(1.07-1.13)	<.0001
Number of SCD-related outpatient visits (ref: <=4)			
5-9	2.85	(1.85-4.39)	<.0001
>=10	3.68	(2.36-5.76)	<.0001

- DMT users were more likely to be in 13-17 age groups (reference: 5-12 years).
- Compared to non-users, DMT users were associated with more SCD-related outpatient visits and VOC episodes and had higher odds of using hydroxyurea in the pre-index period.

DISCUSSION

- As of the end of 2021, the uptake of newly approved DMTs remains low. Potential causes include a lack of clinical guidelines and high drug prices.
- At the patient level, the use of the newly approved DMTs was associated with the severity of disease (more VOC events) and previous greater healthcare utilization (hydroxyurea use, SCD-related outpatient visits).
- Although the newly approved DMTs are not eligible for children at a young age, overall, the use of the newly approved DMTs was associated with being adolescents or young adults.
- In the future, the association between more clinical characteristics (number of ED visits, number of in-hospital stays, number of SCD-related comorbidities) and the use of newly approved DMTs will be examined.

REREFENCFE

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