Prescribing Trends of Newly Approved Sickle Cell Disease-Modifying Medications

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Yahan Zhang[1], Hyeun Ah Kang[1], Robert C. Mignacca[2,3], Alicia Chang[2,3]

[1]Health Outcomes Division, College of Pharmacy, The University of Texas at Austin, Austin, TX
[2] Children's Blood and Cancer Center at Dell Children's Hospital, Austin, TX
[3] Department of Pediatrics, Dell Medical School, The University of Texas at Austin, TX

The University of Texas at Austin College of Pharmacy

INTRODUCTION

Sickle cell disease (SCD) is a rare, inherited monogenetic blood disorder that disproportionately affects Blacks and African Americans.

- Approximately 100,000 individuals in the United States are estimated to be affected by SCD.[1]
- Over 90% of the patients in the U.S. are Black or African-American, and about 5% of the patients are Hispanic.[1]
- Sickle cell disease patients may experience a series of acute and chronic complications, which results in high healthcare resource utilization.
- Compared to the general population, SCD patients have an over 20 years shorter life expectancy.[2]
- 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.
- Since 2017, three new medications, including L-glutamine, crizanlizumab-tmca, and voxelotor have been approved as additional options for SCD.

Drug	Eligible age	Approval date	Mechanism of action[4]
Hydroxyurea[a]	>= 18 years >=2 years	03/04/1998 12/21/2017	Increase feta hemoglobin Reduction in red cell adhesion Reduction in white blood cells and platelets
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

[a]Hydroxyurea has been widely prescribed for patients younger than the eligible age as off-label use before the FDA approval. The NHLBI recommended hydroxyurea for patients 9 months and older in their 2014 guideline.[5]

OBJECTIVE

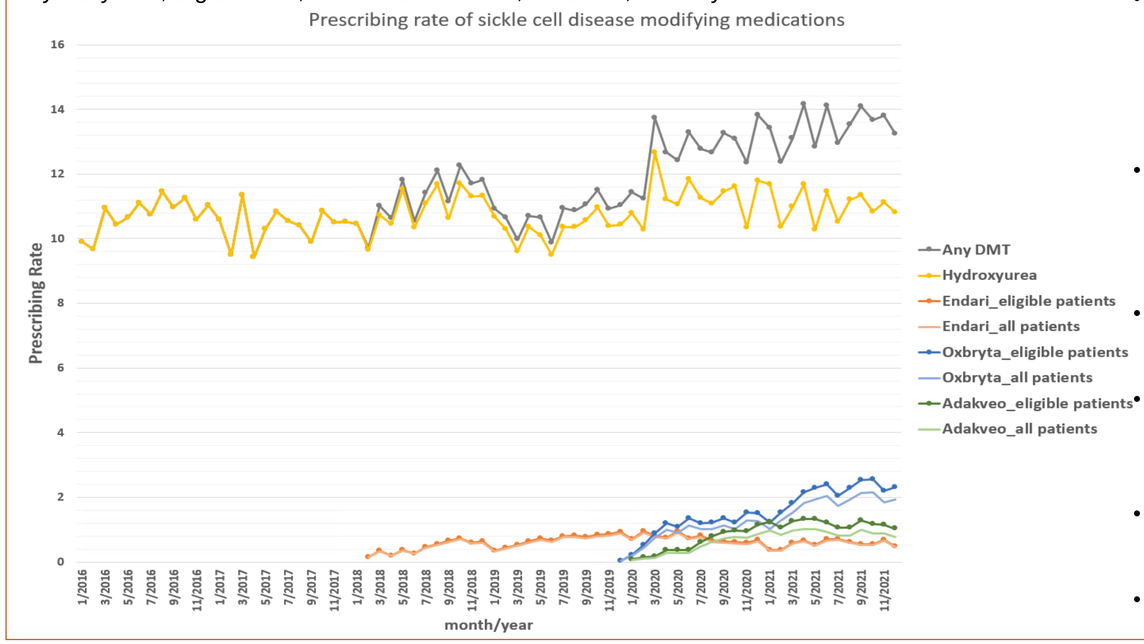
- Data on real-world use of newly approved DMTs are limited.
- The objective of this study is to characterize trends in dispensing the newly approved SCD disease-modifying medications, including L-glutamine, crizanlizumab, and voxelotor, in addition to hydroxyurea.
  - To describe the number of patients who had at least one filled prescription.
  - To describe the dispensing rate of each type of DMTs among total SCD patients and eligible patients by month.

METHOD

- **Study design**
- Retrospective, longitudinal cohort study
- **Data source**
- 2016-2021 Merative™ MarketScan Commercial Database
- **Inclusion/exclusion criteria**
- Patients had ≥1 inpatient or ≥2 outpatient visits with an SCD ICD-10 diagnosis code on separate dates.
- Age between 2-64 years old.
  - The drug-specific eligible patient: hydroxyurea (2-64 years); L-glutamine (5-64); Crizanlizumab (16-64); Voxelotor (12-64).
- Patients without pharmacy coverage were excluded.
- Patients with a cancer diagnosis were excluded.
- **Statistics:** The monthly dispensing rate was calculated using the number of patients who had at least one prescription each month divided by the number of monthly enrollees who met the inclusion criteria.

RESULTS

- A total of 12,378 patients (mean [SD] age = 29.5 [16.4], 59.3% female) were eligible for the analysis.
- From 2016 to 2021, 3,051, 221, 101, 196, and 3,129 patients had ≥1 prescription filled for hydroxyurea, L-glutamine, crizanlizumab-tmca, voxelotor, and any DMTs.



- Approximately 74.7% of the SCD patients had no fill for any DMT during the study period.
- Monthly dispensing rates of the total SCD population for hydroxyurea L-glutamine, crizanlizumab-tmca, voxelotor, and any DMTs in 12/2021 were 10.81%, 0.46%, 0.78%, 1.94%, and 13.24%, respectively.
- Monthly dispensing rates of the age-eligible population for hydroxyurea, L-glutamine, crizanlizumab-tmca, voxelotor in 12/2021 were 10.81%, 0.48%, 1.03%, and 2.30%, respectively.
- The dispensing rate of hydroxyurea remains stable from 2016-2021, with a 1-2% fluctuation.
- L-glutamine dispensing rates increased slightly after approval but declined a bit after the newer medications became available.
- Crizanlizumab dispensing rates remained stable after a slight increase following approval.
- Voxelotor dispensing rates have gradually increased since approval.

DISCUSSION

- Between 2016 to 2021, the dispensing rates of DMTs increased slightly, especially after the approval of crizanlizumab-tmca and voxelotor. However, the overall prescribing rates of newly approved DMTs were still low.
- More active adoption of novel treatment options is important to improve patient outcomes.
- In the future, more detailed real-world utilization patterns (e.g., persistence, add-on, discontinuation, switching) and the association of patient characteristics will be examined.

REFERENCE

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