

JESSICA BALDWIN,<sup>1</sup> CHUKA UDEZE,<sup>1</sup> NANXIN LI,<sup>1</sup> LYES BOULMERKA,<sup>2</sup> LILA DAHAL,<sup>1</sup> GIANCARLO PESCE,<sup>3</sup> NADIA QUIGNOT,<sup>3</sup> HENG JIANG,<sup>3</sup> FRÉDÉRIC GALACTÉROS<sup>4</sup>

<sup>1</sup>Vertex Pharmaceuticals Incorporated, Boston, MA, USA | <sup>2</sup>Formerly of Vertex Pharmaceuticals Incorporated, Boston, MA, USA | <sup>3</sup>Certara France, Paris, France | <sup>4</sup>Sickle Cell Referral Center, Internal Medicine Unit, Henri Mondor Hospital, Assistance Publique-Hôpitaux de Paris, France

INTRODUCTION

- Sickle cell disease (SCD) is a genetic disorder characterized by expression of abnormal sickle hemoglobin, which leads to a variety of acute and chronic complications<sup>1-3</sup>
- Vaso-occlusive crises (VOCs), a hallmark clinical feature in patients with SCD, cause debilitating pain and can lead to additional organ complications and increased mortality<sup>1,2,4,5</sup>
- There are limited data on healthcare resource utilization (HCRU) in patients with SCD with recurrent VOCs (defined as experiencing ≥VOCs/year for 2 consecutive years) in France

OBJECTIVE

- To describe the HCRU of patients with SCD with recurrent VOCs in France

METHODS

Study Design and Database

- A longitudinal, retrospective cohort study design utilized the French National Health Data System database, Système National des Données de Santé (SNDS), to identify patients with SCD with recurrent VOCs
- The SNDS is a national claims database that captures pseudonymized, longitudinal data for ~99% of the French population, inclusive of overseas territories and reports claims data for 65 million insureds<sup>6</sup>
  - The SNDS contains details of all primary care, hospital, and pharmacy records reimbursed in France
- The study was conducted from January 1, 2012, to March 1, 2020, and included a 7-year eligibility period (from January 1, 2012, to March 1, 2019) and a minimum follow-up of 1 year after inclusion

Patient Identification

- Patients were included in the analysis if they met the following inclusion criteria:
  - At least 1 inpatient claim or registration in the long-term disease (LTD) database with a diagnosis of SCD between January 1, 2012, and March 1, 2019
  - At least 2 VOCs/year in any 2 consecutive years after the first qualifying SCD diagnosis record between January 1, 2012, and March 1, 2019
    - A VOC was defined as an inpatient claim with a relevant diagnosis of SCD with crisis, priapism, or acute chest syndrome
  - At least 12 months of follow-up data after and including the index date
- Patients were excluded if they met the following exclusion criterion:
  - Evidence of hereditary persistence of fetal hemoglobin or hematopoietic stem cell transplant at any time in their medical records
- The index date was the date of the second VOC record in the second year of 2 consecutive years
- All patients were followed for at least 12 months from the index date until death or the end of the study period (March 1, 2020)

Study Measures and Analysis

- Descriptive analyses were conducted for demographics and HCRU for patients with SCD with recurrent VOCs
  - Mean (standard deviation [SD]) values were reported for continuous variables and frequencies/proportions (n [%]) for categorical variables
  - In all cases where data were available for <10 patients, values were masked to protect patient confidentiality
- Demographics, including age, sex, and area of residence, were assessed at the index date
- Rates of VOCs and HCRU (per patient per year [PPPY]) were summarized during follow-up
  - Descriptive analyses of HCRU during follow-up were also conducted for prespecified subgroups

Subgroup Analyses

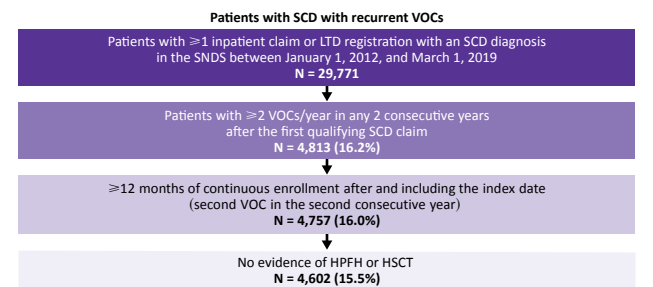
- Descriptive analyses for HCRU were conducted for 2 prespecified subgroups, identified based on the following criteria:
  - VOC frequency during follow-up (<2 and ≥2 VOCs PPPY)
    - Patients with ≥2 VOCs were further categorized into the following subgroups: 2 to <4, 4 to <6, 6 to <8, 8 to <10, and ≥10 VOCs PPPY
  - Age (years) at the index date (0–11, 12–35, and ≥36)

RESULTS

Patient Demographics

- A total of 4,602 patients with SCD with recurrent VOCs were identified in the SNDS (**Figure 1**)

Figure 1. Patient Attrition\*



HPFH, hereditary persistence of fetal hemoglobin; HSCT, hematopoietic stem cell transplant; LTD, long-term disease; SCD, sickle cell disease; SNDS, Système National des Données de Santé; VOC, vaso-occlusive crisis.  
\*Values presented in parentheses represent the proportion of total number of patients with ≥1 inpatient claim or LTD database registration during the study period.

- The mean age of patients with SCD with recurrent VOCs was 19.8 years (SD 13.5; range: 1–76), and 51.8% of patients were female (**Table 1**)
- Most patients (85.6%) lived in metropolitan France, approximately half of whom (53%) lived in the broad Paris area (Île-de-France) and 13.5% of whom lived in Overseas France (**Table 1**)

Table 1. Baseline Demographics

Patients With SCD With Recurrent VOCs (N = 4,602)	
Age, years, mean (SD; range)	19.8 (13.5; 1–76)
Age categories (years), n (%)	
0–11	1,561 (33.9)
12–35	2,464 (53.5)
≥36	577 (12.5)
Female, n (%)	2,384 (51.8)
Broad area of residence, n (%)	
Metropolitan France	3,940 (85.6)
Overseas France	621 (13.5)
Unknown	41 (0.9)
LTD registration, n (%) <sup>a</sup>	4,202 (91.3)
With SCD code	4,089 (88.9)
Follow-up time, years, mean (SD; range)	4.4 (1.8; 1.0–7.2)

LTD, long-term disease; SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.  
\*Patients were registered to this database with the corresponding ICD-10 code for the disease that required long-term and/or expensive treatment due to its severity and/or chronic nature

HCRU

- Patients with SCD with recurrent VOCs experienced an average of 3.8 VOCs PPPY during follow-up (**Table 2**)
- Patients with SCD with recurrent VOCs averaged 13.4 outpatient prescriptions, 6 emergency room (ER) visits, 6.6 outpatient visits, and 5.7 inpatient admissions PPPY (**Table 2**)
  - Of the 5.7 inpatient admissions PPPY, 2.9 were for <1 day and 2.9 were for ≥1 day
  - On average, patients spent 20.8 total days PPPY in the inpatient hospital setting

Table 2. HCRU

Patients With SCD With Recurrent VOCs (N = 4,602)	
HCRU, Mean Rate PPPY (SD)	
Outpatient prescriptions	13.4 (9.9)
Outpatient visits	6.6 (6.0)
External consultations at hospital	3.8 (2.8)
Visits outside hospital	2.8 (4.5)
ER visits	6.0 (4.2)
Not followed by inpatient admission	3.8 (2.8)
Followed by inpatient admission	2.2 (2.8)
Inpatient admissions	5.7 (7.7)
Day cases (<1 day)	2.9 (7.0)
Overnight stays (≥1 day)	2.9 (2.9)
Total days hospitalized	20.8 (25.5)
VOCs	3.8 (3.6)

ER, emergency room; HCRU, healthcare resource utilization; PPPY, per patient per year; SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

Subgroup Analyses: HCRU

- Patients with a higher number of VOCs during follow-up had higher HCRU, driven by high inpatient admission rates PPPY (≥2 VOCs: 7.5; <2 VOCs: 2.6) (**Table 3**)
- HCRU increased as patient age increased; patients in the oldest age cohort (≥36 years) had the highest rates PPPY of outpatient prescriptions (19.5), outpatient visits (9.2), and inpatient admissions (7.9) (**Table 3**)

Table 3. Subgroup Analyses: HCRU by Number of VOCs and Age

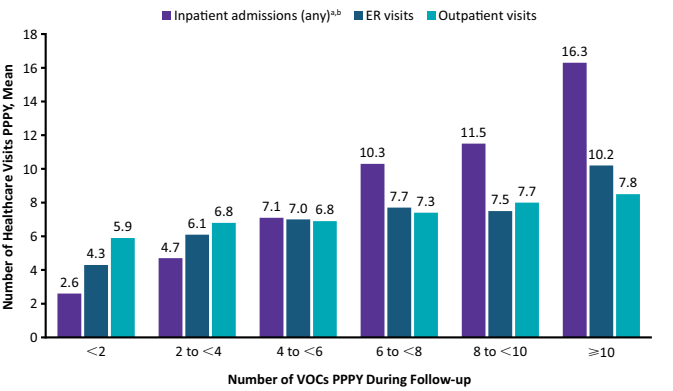
HCRU, Mean Rate PPPY (SD)	VOCs PPPY		Age Group		
	<2 (n = 1,638)	≥2 (n = 2,964)	0–11 Years (n = 1,561)	12–35 Years (n = 2,464)	≥36 Years (n = 577)
Outpatient prescriptions	12.2 (8.8)	14.1 (10.4)	13.1 (5.2)	12.2 (10.7)	19.5 (13.1)
Inpatient admissions	2.6 (5.2)	7.5 (8.3)	4.8 (3.9)	5.8 (6.8)	7.9 (14.9)
Overnight stays (≥1 day)	1.3 (1.1)	3.8 (3.1)	2.5 (2.2)	3.2 (3.3)	2.3 (2.5)
Day cases (<1 day)	1.4 (5.0)	3.7 (7.7)	2.3 (3.3)	2.6 (5.8)	5.6 (14)
Total days hospitalized	8.9 (14.4)	27.4 (27.8)	15.8 (15.7)	23.2 (26.9)	24.0 (36.4)
Outpatient visits	5.9 (5.0)	7.0 (6.4)	5.6 (3.4)	6.6 (6.2)	9.2 (7.5)
External consultations at hospital	3.4 (2.4)	4.0 (3.0)	3.6 (2.1)	3.7 (2.9)	4.9 (3.8)
Visits outside hospital	2.5 (4.0)	2.9 (4.8)	2.0 (2.4)	3.0 (5.2)	4.3 (6.1)
ER visits	4.3 (2.5)	7.0 (4.7)	5.6 (3.0)	6.3 (4.9)	6.1 (4.2)
Not followed by inpatient admission	3.4 (2.4)	4.0 (3.0)	3.6 (2.1)	3.7 (2.9)	4.9 (3.8)
Followed by inpatient admission	0.9 (0.7)	3.0 (3.2)	2.0 (1.6)	2.6 (3.4)	1.2 (1.5)

ER, emergency room; HCRU, healthcare resource utilization; PPPY, per patient per year; SCD, sickle cell disease; SD, standard deviation; VOC, vaso-occlusive crisis.

Subgroups Analyses: HCRU (Continued)

- Higher numbers of VOCs were positively correlated with higher rates of inpatient admissions, ER visits, and outpatient visits (**Figure 2**)

Figure 2. Subgroup Analyses: HCRU by Number of VOCs



ER, emergency room; HCRU, healthcare resource utilization; PPPY, per patient per year; VOC, vaso-occlusive crisis.  
\*Number of inpatient day cases (mean PPPY) by VOC number category: <2 (1.4); 2 to <4 (2); 4 to <6 (3); 6 to <8 (5.4); 8 to <10 (7); ≥10 (8.7).  
\*Number of inpatient overnight stays (mean PPPY) by VOC number category: <2 (1.3); 2 to <4 (2.7); 4 to <6 (4); 6 to <8 (4.9); 8 to <10 (4.5); ≥10 (6.6).

LIMITATIONS

- As with any claims database analysis, this study utilized ICD-10 codes to identify patients with SCD with recurrent VOCs and was thus subject to misclassification bias due to inaccurate coding; however, the effect of this bias was limited, given the additional requirements for inclusion (e.g., 2 VOCs in 2 consecutive years)
  - HCRU from the actual use of some treatments was likely underestimated, as prescriptions administered during hospital stays were not documented (unless the drugs prescribed were classified as expensive drugs)
- Patients with SCD who have recently emigrated to France might be overrepresented in the 1% of the French population not recorded in the SNDS
- Given the minimum 12-month post-index period for patients with SCD, individuals who died during this period were excluded, which could have further led to an underestimation of HCRU

CONCLUSIONS

- Patients with SCD with recurrent VOCs had substantial HCRU in France, driven by frequent outpatient prescriptions, outpatient visits, ER visits, and inpatient admissions
- Higher numbers of VOCs and older age were associated with higher HCRU
- Elevated HCRU in patients with SCD with recurrent VOCs highlights the need for innovative therapies in this space

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AUTHOR DISCLOSURES

JB, CU, NL and LD are employees of Vertex Pharmaceuticals Incorporated and may hold stock or stock options in the company. LB is a former employee of Vertex Pharmaceuticals and may hold stock or stock options in the company. GP, NQ, and HJ are employees of Certara France and may hold stock or stock options in the company. FG is an employee of the Sickle Cell Referral Center, Henri Mondor Hospital Paris, France. Approval for use of SNDS data was granted by all relevant authorities and governing bodies. Analyses for this study were performed through remote access on the Caisse Nationale de l'Assurance Maladie (CNAM) portal to comply with national security guidance (Le Référentiel de Sécurité). The final protocol was reviewed and approved by a scientific committee and the National Informatics and Liberty Commission (CNIL, decision DR-2022-065, March 2, 2022). All patient data were pseudonymized, which according to applicable legal requirements renders the data exempt from privacy laws; therefore, obtaining informed consent from patients was not required. The interpretation and conclusions contained in this study are those of the authors alone.