Drug Utilization Patterns among Patients Hospitalized with COVID-19 in the United States (January 2021 – February 2022)

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Abstract

This cohort study describes utilization patterns for corticosteroids (CS), interleukin-6 inhibitors (IL-6i), Janus kinase inhibitors (JAKi), and remdesivir (RDV) among hospitalized adults with COVID-19 admitted from January 1, 2021 through February 1, 2022 (N = 51,066), overall and by respiratory support required. Data included claims and hospital chargemaster data (HealthVerity) to allow for capture of inpatient treatment with CS, IL-6i, JAKi, and RDV. The number and distribution of patients were reported for up to the first three drug/drug regimen lines initiated. Pharmacological management of patients was generally in line with the National Institutes of Health (NIH) COVID-19 treatment guidelines. However, the treatment patterns observed suggest that prescribing preference and potential confounding by indication should be considered in the design and interpretation of comparative effectiveness studies. Studies of drugs often initiated later in hospitalization (i.e., IL6-is and JAKis) should also consider prior/concomitant use of other therapeutics as potential confounders.

Introduction

Understanding longitudinal drug utilization patterns for patients hospitalized with COVID-19 is important for developing methods to evaluate the effectiveness of COVID-19 therapeutics using real-world data and to inform the ability of clinical practice to respond to the evolving availability of treatments and therapeutic guidelines. In April 2021 and July 2021, the NIH COVID 19 treatment guidelines were revised to include IL-6i and JAKi, respectively, as add-in therapy to dexamethasone or other systemic CS for patients with severe or critical COVID-19 disease. At the time of this study's implementation, no published drug utilization studies included the period during and after the addition of both IL-6i and JAKi. The objective of this study was to describe utilization patterns for CS, IL6-i, JAKi, and RDV among hospitalized adult patients with COVID-19 from January 2021 to February 2022 during the entire patient's hospitalization; during periods within the hospitalization categorized by respiratory support requirement (RSR); and over calendar time.

Materials and Methods

This observational cohort study describes drug utilization in adult patients hospitalized with COVID-19 using HealthVerity Hospital Chargemaster and Claims healthcare data, comprising medical and pharmacy open and closed claims, and inpatient and outpatient hospital billing data.

Patients eligible for inclusion in the study population were all those aged 18-84 years who had an inpatient hospital chargemaster event between January 1, 2021, and February 1, 2022, and a diagnosis of COVID-19 (ICD-10 code U07.1) at admission, or within the 7 days prior. Patients with missing age or sex, or without continuous medical claims enrollment during the 183-day (baseline period) before admission (60-day allowable gap) were excluded, to ensure observability.

Exposures to incident drug regimens of interest were described from admission through death, discharge, or 28 days of hospitalization. For each day of a patient's hospitalization, drug events for CS, IL6-i, JAKi, and RDV were sourced from procedure codes (HCPCS/CPT-4, ICD-10-PCS), and free-text fields from the inpatient chargemaster data. A 183-day washout was applied to capture only incident drug use, and continuous overlapping episodes for each drug or drug class were considered combination regimen.

Results and Discussion

Patients were excluded from the analytic cohort if they were not hospitalized between January 2021 and February 2022 (42.0%); had no medical claims enrollment in the baseline period (20.5%); had no COVID-related diagnosis at hospitalization, or within 7 days prior to hospitalization (32.8%); had missing age or sex (<0.1%); or were less than 18 or greater than 84 years of age (8.5%).

Initiators of treatments of interest were as follows: CS monotherapy (33.3%); IL6-i monotherapy (0.6%); JAKi monotherapy (0.2%); RDV monotherapy (4.5%); CS+RDV (32.9%); IL6-i+CS (5.3%); JAKi+CS (4.5%); JAKi+RDV (0.2%); IL6-i+RDV (0.1%); IL6-i+JAKi (0.0%); JAKi+CS+RDV (4.1%); IL6-i+CS+RDV (3.8%); IL6-i+JAKi+CS+RDV (0.3%); IL6-i+JAKi+CS (0.2%); IL6-i+JAKi+RDV (0.0%).

Hospitalized Cohort, N = 51,066 (100.0%)			
Demographic & Clinical		**Baseline Clinical Characteristics**	
Age		**Comorbidity Index**	
...mean (sd)	52.5 (16.6)	...mean (sd)	3.1 (3.3)
...median [IQR]	55 [39, 65]	...median [IQR]	2.0 [1.0, 5.0]
Sex		**Overweight/Obese; n (%)**	19,174 (37.5%)
...Female; n (%)	28,076 (55.0%)	**Chronic Kidney Disease; Diabetes; n (%)**	10,084 (19.7%) 16,765 (32.8%)
U.S. Census Region		**Cardiovascular disease ;**	30,082 (58.9%)
...Northeast; n (%)	10,529 (20.6%)	**Immunosuppressed; n**	14,080 (27.6%)
...Midwest; n (%)	4,016 (7.9%)	**Mental**	11,644 (22.8%)
...South; n (%)	24,364 (47.7%)	**Smoking/Tobacco; n (%)**	14,956 (29.3%)
...West; n (%)	12,153 (23.8%)	**Neurological**	5,410 (10.6%)
...Other/Missing; n (%)	4 (<0.1%)	**Hospital Characteristics**	
Insurance Type		**Hospital Setting**	
...None recorded; n (%)	424 (0.8%)	...Urban; n (%)	45,146 (88.4%)
...Commercial only; n (%)	14,393 (28.2%)	...Rural; n (%)	4,568 (8.9%)
...Medicare; n (%)	10,030 (19.6%)	...Other/Missing; n (%)	1,352 (2.6%)
...Medicaid; n (%)	26,219 (51.3%)		

Table 1. Select demographic, clinical, baseline, and hospital characteristics for hospitalized cohort

Among 1,119,940 patients in the data, 51,066 patients were included in the analytic cohort (**Table 1**). Over half of the patients in the cohort (60.6%) were admitted after both JAKi and IL6-i had been added to the NIH guidelines after July 8, 2021 (**Fig. 1).** The most common drug regimens initiated were CS monotherapy (33.3%) and CS+RDV (32.8%). Nearly all of the IL-6i use was tocilizumab (98.7% and 99.4% of IL6-i+CS and IL6-i+CS+RDV initiators), and nearly all of the JAKi use was baricitinib (99.9% and 99.7% of JAKi+CS and JAKi+CS+RDV initiators). Few patients initiated IL-6i+CS (5.3%), RDV (4.5%), JAKi+CS (4.5%), JAKi+CS+RDV (4.1%), and IL-6i+CS+RDV (3.8%). All other combinations of interest were each observed in <1% of the cohort.

Over half of patients (57.7%) received at least one incident drug regimen of interest during their hospitalization; the remaining patients (42.3%) never received an incident drug regimen of interest during hospitalization. The most common first-line regimens were CS+RDV (25.1%) and CS alone (23.4%). These drug regimens comprised a similar proportion of second-line therapies but were less commonly observed third-line.

RDV was the next most common first-line regimen (4.4%), though remdesivir monotherapy was uncommon in later lines of treatment. Regimens that include IL-6i and JAKis were more common in later drug treatment regimen lines after other drugs (largely CS and CS+RDV) were first administered. A similar number of patients initiated IL-6i combination regimens and JAKi regimens across all treatment lines (0.8% initiated first-line IL-6i and first-line JAKi combinations, 5.2% and 4.6% initiated second-line IL-6i and JAKi combinations, and 18.1% and 14.7% initiated third-line IL-6i and JAKi combinations, respectively) (**Fig. 2**).

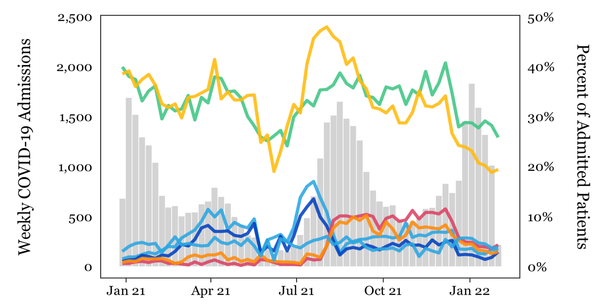


Figure 1. Number and percent of weekly admissions treated with a drug regimen

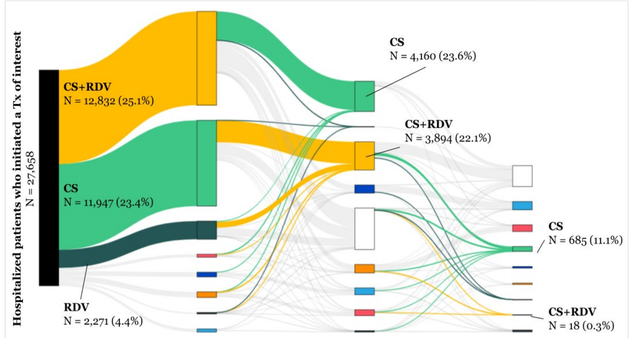
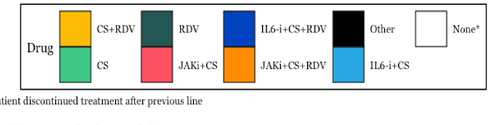


Figure 2. Hospitalized patients receiving at least one drug of interest (N = 27,658 [57.7%])



Key for Figures 1, 2, and 3

Combinations that included JAKis were more common than combinations. that included IL-6is across nearly all treatment lines during hospitalization time on O2. Conversely, IL6-i combinations were more common than JAKi combinations across all drug regimen lines during hospitalized time on NIV/HFO and IMV/ECMO.

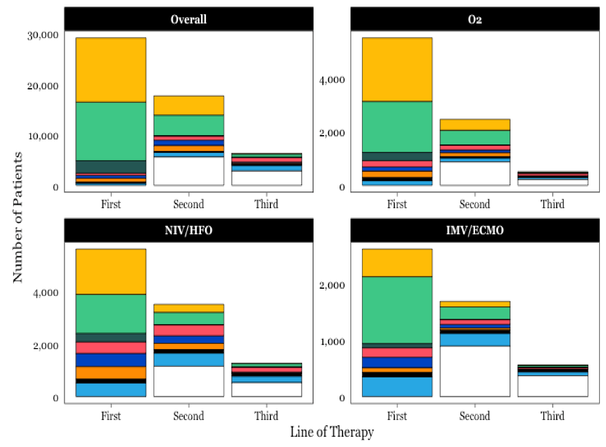


Figure 3. Proportions of hospitalized COVID-19 patients on treatments of interest over hospitalization time, stratified by RSR

Across all RSRs, CS and CS+RDV were the most common first-line regimens. Second-line CS and CS+RDV were most common among patients receiving O2; third-line CS was most common among patients receiving O2 and NIV/HFO. Remdesivir monotherapy was primarily a first-line drug regimen and was most common among O2 and NIV/HFO patients (**Fig. 3**).

Conclusion

The study findings suggest that inpatient COVID-19 treatment prescribing was generally in line with the NIH COVID-19 treatment guidelines. JAKi combinations were more commonly used during hospitalization-time characterized by receipt of O2, while IL-6i combinations were more commonly used during receipt of NIV/HFO and IMV/ECMO. Notably, JAKi combinations were observed during receipt of IMV/ECMO, counter to guidelines at the time. Differences between JAKi and IL-6i with regard to use during receipt of O2 and NIV/HFO were unanticipated, since both drug regimens were recommended for these patient subgroups during the study period. Prescribing preference, access to drug regimens, and potential confounding by indication even within respiratory support requirements levels should be considered in the design and interpretation of future comparative studies. In the meantime, descriptive drug utilization studies should continue to be prioritized to support future comparative studies extending through 2022 and beyond.