Comorbidity burden in patients with COVID-19 treated with molnupiravir in the United States

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Abstract

Individuals with certain medical conditions, eg, diabetes, heart disease, and/or lung disease, are at higher risk of severe COVID-19. Molnupiravir, an oral antiviral drug for treatment of mild-to-moderate COVID-19 in certain adults, was granted US FDA emergency use authorization. Retrospective analyses of US patient-level medical and pharmacy claims and hospital chargemaster data, aggregated by HealthVerity, was conducted. Adults (≥18 years) were indexed to their first outpatient pharmacy fill for molnupiravir between December 24, 2021 and May 2, 2022. Comorbidities were identified using ICD-10 diagnosis, CPT, and/or HCPCS codes during the pre-index period (back to December 1, 2018) and comedications by generic name (from NDCs) ≤90 days before index. Demographic, comorbidity, and comedication characteristics were reported using descriptive statistics. The analyses included 26,191 patients: mean age 58.7 (SD 16.3) years, 59.0% female, with 75.9% residing in the South. Presence of ≥1 comorbidity associated with severe COVID-19 was observed in 87.0%: hypertension (52.5%), overweight/obesity (37.4%), mood disorder (30.7%), and cardiovascular disease (18.9%). Diabetes mellitus was observed in 6944 (26.5%) patients: mean age 62.5 (SD 14.3) years and 54.4% female. Polypharmacy (≥5 comedications) within the last 90 days was also prevalent in both the overall patient population (49.7%) and in patients with diabetes (66.1%). Concomitant use of comedications contraindicated with ritonavir-based COVID-19 treatment was noted in 33.7% of all patients and 45.8% of patients with diabetes. The majority of COVID-19 patients treated with molnupiravir in clinical practice were at high risk of severe COVID-19. Future research needs to assess the impact of molnupiravir on clinical outcomes in real-world practice, including in patients with comorbid conditions.

Clinical outcomes following treatment initiation with molnupiravir were analyzed since the abstract was submitted, and the data are reported in this presentation.

Background

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and, as of June 6, 2022 has led to more than 6.2 million deaths worldwide.[1] Individuals with certain medical conditions, e.g., diabetes, heart disease, and/or lung disease, are at higher risk of severe COVID-19.[2] Molnupiravir (MOV), an orally bioavailable ribonucleoside analog with broad-spectrum antiviral activity against SARS-CoV-2, was granted emergency use authorization by the US FDA for treatment of mild-to-moderate COVID-19 in adults at high risk for progression to severe clinical outcomes. Published MOV phase 3 clinical trial (MOVe-OUT) data demonstrated significant clinical benefit of MOV in reducing the risk of hospitalization and death in patients with mild-to-moderate COVID-19, with a similar safety profile vs placebo.[3] Since the clinical trial was conducted, COVID-19 epidemiology has evolved, including dominance of a new variants and increases in prevalence of vaccination.

Objectives

Among adult patients with evidence of treatment with MOV initiated in a non-hospital setting,

1. To describe demographic, clinical, and treatment characteristics
2. To assess hospitalization and healthcare resource utilization over a 28-day follow-up period

Methods

Data source: Patient-level medical and pharmacy claims, hospital chargemaster data, laboratory data, and COVID-19 vaccination data, aggregated by HealthVerity.

Study design

A retrospective analysis of adults (≥18 years) with outpatient pharmacy fill for MOV (index date). At least 1 medical claim in the baseline period and at least 1 pharmacy claim in the prior 14 months were required (Figure 1).

Figure 1. Study Design

MOV=molnupiravir. †MOV granted emergency use authorization by US FDA. ‡ Index date not included in the follow-up period.

Exclusions were having any hospitalization on index date, any COVID-related hospitalization in the 30 days prior to index, or evidence of being pregnant or delivering within the 90 days prior to index (Cohorts 1 and 2). Additionally, those who used antivirals other than MOV in the 30 days prior to index date or those having a diagnosis for post-COVID condition (diagnosis code: U09.9) in baseline were excluded from assessment of hospitalization in the follow-up period (Cohort 2).

Study measures

- *Cohorts 1 & 2:* Comorbidities were identified using International Classification of Disease, 10th Revision, Clinical Modification (ICD-10-CM), Current Procedural Terminology (CPT), and/or Healthcare Common Procedure Coding System (HCPCS) codes during baseline period (back to December 1, 2018)
- *Cohorts 1 & 2:* Comedications were identified by generic name (from National Drug Codes [NDC]) on or within 90 days before the index date). Risk of a potential drug-drug interaction (pDDI) of any comedications metabolized through the CYP3A4 isoenzyme pathway with ritonavir was categorized as contraindicated and major pDDI[4,5,6]
- *Cohort 2:* Hospitalization, inpatient resource use (intensive care unit [ICU], oxygen administration, invasive mechanical ventilation [IMV], extracorporeal mechanical oxygenation [ECMO]), and outpatient resource use [emergency room, office and telephone visit, COVID-19 laboratory test]) were assessed over a 28-day follow-up period using CPT, revenue, and place-of-service codes

Statistical analyses: Descriptive statistics were used to report data for the overall population and stratified by diabetes mellitus. Aetion Evidence Platform® was used for analyses.

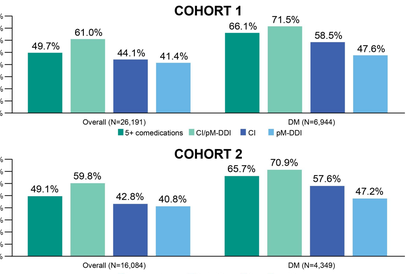
Results

Table 1. Patient characteristics

Characteristics	COHORT 1		COHORT 2	
	Overall	DM	Overall	DM
N	26,191	6,944	16,084	4,349
Age, mean [SD]	58.7 (16.3)	62.5 (14.3)	57.6 (16.1)	61.4 (14.2)
Age group, n (%)				
18-39	3,403 (13.0%)	387 (5.6%)	2,268 (14.1%)	272 (6.3%)
40-49	3,857 (14.7%)	814 (11.7%)	2,561 (15.9%)	557 (12.8%)
50-59	5,836 (22.3%)	1,656 (23.8%)	3,726 (23.2%)	1,075 (24.7%)
60-69	6,322 (24.1%)	1,967 (28.3%)	3,798 (23.6%)	1,229 (28.3%)
70+	6,773 (25.9%)	2,120 (30.5%)	3,731 (23.2%)	1,216 (28.0%)
Female, n (%)	15,457 (59.0%)	3,777 (54.4%)	9,392 (58.4%)	2,323 (53.4%)
US Census Region				
South	19,871 (75.9%)	5,249 (75.6%)	13,226 (82.2%)	3,489 (80.2%)
Northeast	1,909 (7.3%)	534 (7.7%)	545 (3.4%)	171 (3.9%)
Midwest	2,256 (8.6%)	601 (8.7%)	1,228 (7.6%)	352 (8.1%)
West	2,067 (7.9%)	514 (7.4%)	1,024 (6.4%)	298 (6.9%)
COVID-19 vaccination†, n (%)				
Vaccinated	8,610 (32.9%)	2,429 (35.0%)	4,909 (30.5%)	1,433 (33.0%)

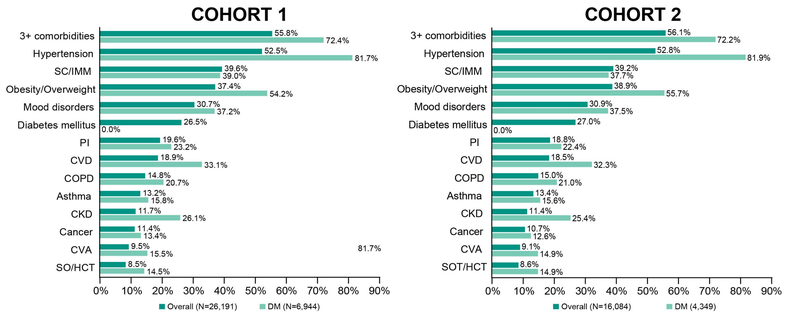
DM=diabetes mellitus; SD=standard deviation.
†As available and identified in baseline period. Based on claims submitted to insurance, selected state registry, and selected vaccination sites where insurance information was not mandatory. Vaccine data in HealthVerity database is estimated to be underreported by ~30%.

Figure 2. Polypharmacy and comedications contraindicated or with potential major drug-drug interaction with ritonavir-containing COVID-19 treatment‡



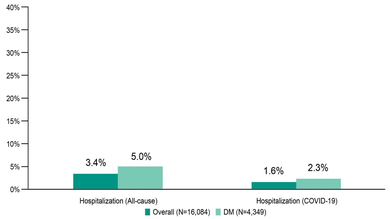
CI=contraindicated; DM=diabetes mellitus; pM-DDI=potential major drug-drug interaction.
‡Comedication (defined as unique generic name) other than molnupiravir. The time period evaluated was the 90 days prior to and including the index date.

Figure 3. Prevalence of selected underlying medical conditions and risk factors associated with high risk of severe COVID-19 outcomes†,1



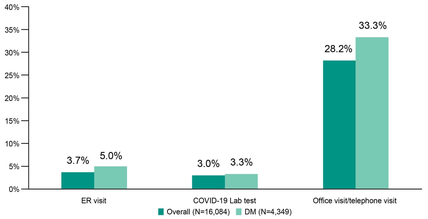
*DM included in assessment for the Overall group but excluded in assessment for the DM group. †Identified during baseline period defined as time period before the index date up to December 1, 2018.
CVA=cerebrovascular accident; COPD=chronic obstructive pulmonary disorder; CKD=chronic kidney disease; CVD=cardiovascular disease; DM=diabetes mellitus; HCT=hemopoietic cell transplantation; IMM=immunosuppressive medications; NA=Not applicable (all [100%] patients in DM group have diabetes mellitus); PI=primary immunodeficiency; SC=systemic corticosteroids; SOT=solid organ transplantation. CVD includes coronary artery disease, heart failure, and cardiomyopathies; Mood disorders include depression and anxiety-related disorders.

Figure 4. Hospitalization over 28-day follow-up after treatment initiation with molnupiravir



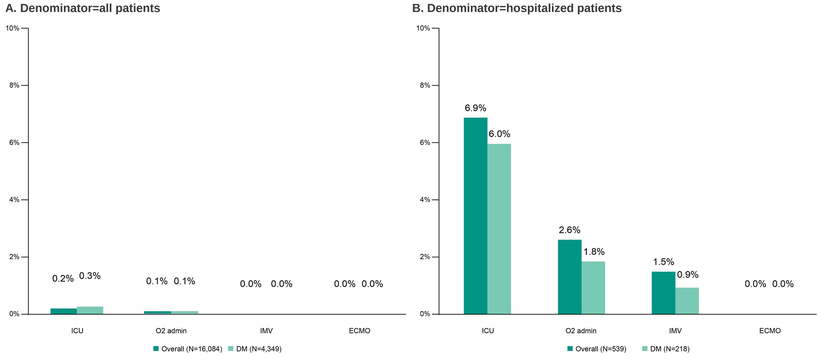
DM=diabetes mellitus.

Figure 5. Outpatient resource use over 28-day follow-up after treatment initiation with molnupiravir



DM=diabetes mellitus; ER=Emergency Room
Note: lab tests are based on claims submitted to insurance and selected laboratory testing data. Available data does not include home testing or testing sites that do not require insurance.

Figure 6: Inpatient resource use over 28-day follow-up after treatment initiation with molnupiravir



ECMO=Extracorporeal membrane oxygenation; ICU=Intensive Care Unit; IMV=Invasive Mechanical Ventilation; O2 admin=Oxygen administration

Discussion

- To our knowledge, this is the first real-world study to assess clinical outcomes following treatment initiation with MOV in the United States
- Among patients treated with MOV,
  - Multimorbidity (3+ conditions) and polypharmacy (5+ products) were commonly observed, with relatively higher prevalence in patients with DM compared to all patients
  - Hospitalization and outpatient resource use after MOV initiation was uncommon (except physician visit); nominally more in patients with DM compared to all patients
  - Among hospitalized patients, intensive care resource use was not prevalent, with slightly lower use in patients with DM; no patients required ECMO
- Completeness and composition of patient-level or open (sourced enroute from providers, not from health insurers) claims data are less stable and may lead to underestimation of hospitalization and related health care resource use
  - Health care encounters from all hospitals that study patients may use for inpatient services may not be captured in this database
  - To minimize concerns around data completeness due to time lag, the assessment of clinical outcomes used only data from at least two months prior to the most available data
- Death information was not available and so was not accounted for in the assessment of clinical outcomes

Conclusion

- The study findings shows that molnupiravir is an effective treatment option for COVID-19 in patients with high risk of severe COVID-19 in real-world clinical practice

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