Chula Med J. January - February 2026;70(1): 39 - 48 **DOI : 10.56808/2673-060X.**5566

Original article

Treatment outcomes and factors associated with treatment failure among patients with mild-to-moderate COVID-19 receiving five-days of oral molnupiravir vs. three-days of intravenous remdesivir in a real-world practice

Sarawut Kittikasemsook[a], Pattama Torvorapanit[b], Chotirat Nakaranurack[c,*]

[a]*Department of Pharmacy, King Chulalongkorn Memorial Hospital, Thai Red Cross, Bangkok, Thailand*
[b]*Thai Red Cross Emerging Infectious Diseases Clinical Center, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand*
[c]*Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand*

Abstract

Background: The initiation of antiviral treatment for coronavirus disease 2019 (COVID-19) is based on the patient's risk of developing severe symptoms. Molnupiravir and remdesivir are new antiviral agents with limited data in real-world practice, especially in Thailand.
Objectives: This study aimed to evaluate the treatment outcomes, adverse drug reactions (ADRs), and factors associated with treatment failure in adults with mild-to-moderate symptoms of COVID-19 who received five days of oral molnupiravir or three days of intravenous remdesivir at treatment initiation.
Methods: This retrospective study was conducted at King Chulalongkorn Memorial Hospital, Thai Red Cross Society. The inclusion criteria were patients 18 years or older with mild-to-moderate symptoms of COVID-19 who were treated during April 2022 and received five days of oral molnupiravir or three days of intravenous remdesivir at treatment initiation. Factors associated with treatment failure were analyzed by logistic regression with statistical significance at $P < 0.05$.
Results: Of the 182 included patients, 105 (57.7%) received remdesivir and 77 (42.3%) received molnupiravir. Treatment failure between the six cases (7.8%) of the molnupiravir group and 24 cases (22.9%) of the remdesivir group was statistically significant ($P = 0.007$). By day 10, 30 patients (39.0%) in the molnupiravir group and 75 patients (71.4%) in the remdesivir group had clinically resolved ($P < 0.001$). Male gender (adjusted odds ratio = 3.4) and pneumonia (adjusted odds ratio = 2.5) were associated with treatment failure. No deaths or rehospitalizations within 30 days after antiviral therapy were observed in this study. The recorded ADRs included headaches or dizziness with remdesivir (3.8%) and diarrhea with molnupiravir (5.2%).
Conclusion: Oral molnupiravir for five days and three days of intravenous remdesivir are still recommended treatments for patients with mild-to-moderate COVID-19 at risk of developing severe symptoms. Both antiviral agents are safe with few and mild ADRs. This study suggests closely monitoring patients with COVID-19 and pneumonia.

Keywords: COVID-19, factors, molnupiravir, three-day intravenous remdesivir, treatment outcomes.

***Corresponding to: Chotirat Nakaranurack,** Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University Bangkok 10330, Thailand.
E-mail: chotirat.n@pharm.chula.ac.th
Received: December 20, 2024
Revised: October 14, 2025
Accepted: November 2, 2025

Novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2), presents with symptoms ranging from mild to severe.[1] There are many studies of antiviral agents for the treatment of COVID-19, but only a few antiviral agents are recommended, depending on the disease severity.[2] From the Infectious Diseases Society of America (IDSA) guidelines on the treatment and management of patients with COVID-19 (IDSA guideline), it is recommended in ambulatory patients with mild-to-moderate COVID-19 at high risk for progression to severe disease that nirmatrelvir/ritonavir treatment be initiated within 5 days of symptom onset rather than no nirmatrelvir/ritonavir treatment.[3] Early intravenous remdesivir started within seven days of symptoms demonstrated clinical results indicating that it could lower COVID-19–related hospitalization or death from any cause by Day 28 among patients (12 years of age or older) with mild-to-moderate COVID-19 who had risk factors for disease progression, compared to a placebo.[4] For severe COVID-19, intravenous remdesivir is the preferred option, which exhibited mortality benefit with a 5–10 day treatment duration.[5, 6] The IDSA guideline suggested molnupiravir for ambulatory patients (≥18 years) with mild-to-moderate COVID-19 at high risk for progression to severe disease who had no other treatment options. Moreover, the IDSA guideline panel suggests molnupiravir initiated within 5 days of symptom onset rather than no molnupiravir treatment.[3] Antiviral agents in Thailand are recommended for patients with COVID-19, depending on the severity of the illness. During the period of nirmatrelvir/ritonavir shortage (2021–2022), multiple drug interaction issues of nirmatrelvir/ritonavir may have limited their use.[7] In practice, molnupiravir and three days of intravenous remdesivir were widely used in Thailand for patients with mild COVID-19 and risk factors of disease progression during that time. Limited previous studies, especially in Thailand, have been conducted on the clinical data comparison between molnupiravir and three days of remdesivir for those patients. Therefore, our study aimed to evaluate the treatment outcomes, rehospitalization, and mortality rate within 30 days after antiviral therapy among patients with COVID-19 who received either molnupiravir or three days of intravenous remdesivir at treatment initiation. Moreover, we provide the comparison data, adverse drug reactions (ADRs), and factors associated with treatment failure.

Materials and methods

This retrospective cohort study was conducted at King Chulalongkorn Memorial Hospital (KCMH), Thai Red Cross Society, an approximately 1,500-bed tertiary referral and teaching hospital in Bangkok, Thailand, for the 1–30 April 2022 period. The inclusion criteria were: 1) patients aged ≥ 18 years with confirmed COVID-19 by real-time polymerase chain reaction (RT-PCR) for SARS-CoV-2; 2) patients with nonsevere symptoms of COVID-19 disease; 3) patients who received either oral molnupiravir (200 mg) 4 tablets every 12 h for five days or intravenous remdesivir (200 mg) once daily on the first day, then 100 mg once daily for the following two days (total duration for three days) at treatment initiation; and 4) patients who received treatment within five days from the symptom onset. Pharmacists followed up with patients on days 2, 5, 10, and 30 after antiviral therapy for treatment failure and ADRs via phone. Patients who decided not to take molnupiravir or for whom the pharmacists could not follow up by phone after hospital discharge within 1 month were excluded from this study. The Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, reviewed and approved this study (IRB no. 0614/65). The primary objective of this study was to assess the rates of treatment failure in patients receiving oral molnupiravir for five days or intravenous remdesivir for three days at treatment initiation. The secondary objectives included identifying factors associated with treatment failure in patients with mild-to-moderate COVID-19 receiving either molnupiravir or remdesivir and describing the ADRs recorded for both medications. The KCMH treatment guideline for molnupiravir or three days of remdesivir prescription was indicated for patients with mild-to-moderate COVID-19 and one or more disease progression risk factors, as detailed in **Table 1**. According to hospital policy, in the group that received remdesivir, all patients were admitted receiving remdesivir for 3 days.

The demographic and clinical data were retrieved from the hospital electronic database (ePHIS™; electronic public health information system), pharmacist data records, routine pharmacist monitoring phone calls, and report charts of the drug-related problems of molnupiravir and remdesivir. Data collection included baseline characteristics, COVID-19 vaccination history, clinical severity, treatment outcomes, and ADRs of molnupiravir and remdesivir.

Mild COVID-19 disease was defined as symptomatic patients (e.g., fever, cough, myalgias, sore throat, nasal congestion, and diarrhea) without evidence of viral pneumonia or hypoxia. Moderate COVID-19 disease was defined as having clinical symptoms of pneumonia but no evidence of severe pneumonia, including SpO_2 ≥ 90.0% on room air. Severe COVID-19 disease was defined as having clinical signs of pneumonia plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO_2 < 90.0% on room air. The patients' clinical severity followed the World Health Organization guidelines.[8] This study's definition of treatment failure included rehospitalization within 30 days after antiviral therapy, switching their regimen from molnupiravir to remdesivir, and extending the duration of remdesivir treatment from 3 days to 5–10 days.

Table 1. Treatment guideline for molnupiravir and three-days remdesivir on COVID-19 Patients received care at King Chulalongkorn Memorial Hospital, Thai Red Cross Society from April 1, 2022, to April 30, 2022 (issued on March 28, 2022).

	Molnupiravir	**Three-days Remdesivir**
Criteria	COVID-19 patients must meet both the following criteria and have no contraindications. - A patient without hypoxia, with an onset of signs and symptoms less than 7 days with age of ≥ 60 years, who can be treated as an outpatient, with one or more of the following risk factors for advanced disease: BMI ≥ 30 kg/m ^{2} or weight > 90 kg CVD/CAD/Congenital heart disease DM (HbA_{1c} > 7.5%) or received insulin CKD GFR 30 - 60 ml/min/1.73 m^2 Chronic liver disease COPD/Chronic lung disease Received high-dose immunosuppressants/immunodeficiency - A history of receiving the last dose of vaccine more than three months prior	COVID-19 patients who are not on oxygen support with an onset of fewer than seven days, a history of receiving only 0-1 dose of vaccine, an age of >60 years, and one or more of the risk factors for advanced disease: - BMI ≥ 30 kg/m ^{2} - CVD/CAD/uncontrolled HTN, - DM (HbA_{1C} > 7.5%), - stage 4 - 5 CKD, cirrhosis, COPD/ chronic lung disease, - HIV with CD4 < 200 cell/mm^3, CVA/neurodevelopment disorder/sickle cell disease, use of high-dose immunosuppressants /immunodeficiency, or an infectious disease specialist deeming that the disease is likely to progress - A patient who has received ≥ 2 doses of vaccine (regardless of the timing of the last dose), with an age of > 75 years or current use of high-dose immunosuppressants or primary immunodeficiency A patient who has received ≥ 2 doses of vaccine (with the last dose received more than 3 months prior) with an age of > 60 years and one or more of the risk factors for advanced disease: BMI ≥ 30 kg/m ^{2} CVD/ CAD/uncontrolled HTN, DM (HbA_{1C} > 7.5%), stage 4 -5 CKD, cirrhosis, COPD/ chronic lung disease, HIV with CD4 < 200 cell/mm^3, CVA/neurodevelopment disorder/ sickle cell disease, use of high-dose immunosuppressants/primary immunodeficiency, or an ID specialist deeming that the disease is likely to progress
Contraindications	Pregnancy GFR < 30 ml/min/1.73 m^2 or on dialysis Low platelet or neutrophil count	Remdesivir is not recommended in individuals with eGFR less than 30 ml/min/ 1.73 m^2 or with ALT greater than 10 times the upper limit of normal.

ALT, alanine aminotransferase; BMI, body mass index; CAD, coronary artery disease; CD4, cluster of differentiation 4; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CVA, cerebrovascular; CVD, cardiovascular diseases; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; HbA1c, hemoglobin A1C; HIV, human immunodeficiency virus; HTN, hypertension.

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows, version 23.0 (SPSS Co., Ltd., Bangkok, Thailand). The mean ± standard deviation (SD), median with interquartile range (IQR), and frequencies were used to describe the patients' baseline characteristics, clinical severity, treatment outcomes, and the ADRs of molnupiravir and remdesivir. The chi-square test was used to compare categorical data between patients receiving molnupiravir and remdesivir. An independent *t*-test was performed to compare continuous data between patients receiving molnupiravir and remdesivir. Logistic regression with enter selection was used to estimate the odds ratios (ORs), adjusted ORs (aORs), and associated 95% confidence interval (CI) for factors associated with treatment failure. Variables with $P < 0.05$ were included in the multivariate analysis. $P < 0.05$ in the multivariate analysis was considered statistically significant.

Results

A total of 182 patients were included in this study, of which 105 and 77 patients were in the remdesivir and molnupiravir groups, respectively **(Figure 1).** All patients in the remdesivir group were hospitalized, while all those in the molnupiravir group received care at home at treatment initiation. Patients' median (IQR) age was 71 (65–80) years, and the mean (SD) body mass index was 24.4 (5.4) kg/m^2. Moreover, 159 patients (87.4%) had comorbidities, and hypertension was the most common comorbidity (45.9%). The number of patients with chronic renal disease and immunodeficiency was significantly higher in the remdesivir-treated group than in the molnupiravir-treated group. The baseline characteristics are presented in **Table 2**.

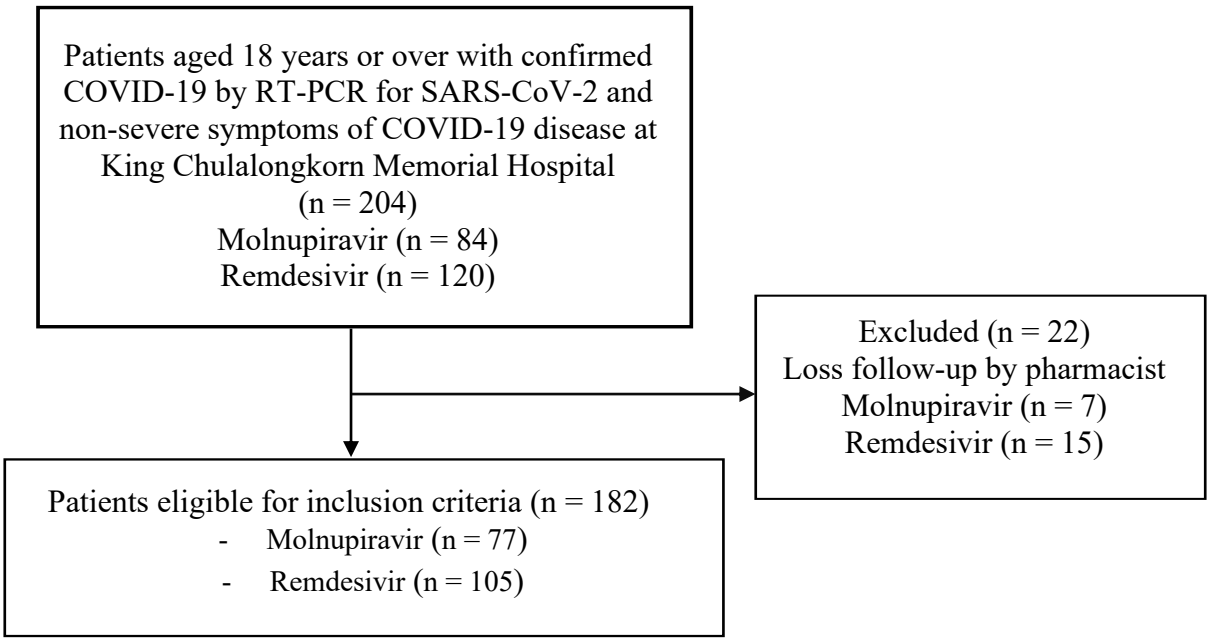

Figure 1. Flow of inclusion. COVID-19, coronavirus disease 2019; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus type 2

Table 2. Baseline characteristic of mild-moderate COVID-19 patients receiving molnupiravir or remdesivir (n = 182).

Characters, n (%)	Total (n= 182)	Molnupiravir (n =77)	Remdesivir (n = 105)	*P*-value
Sex				
Female	97 (53.3%)	41(53.2%)	56 (53.3%)	0.991
Age (years), median (IQR)	71 (65– 80)	71 (67– 78)	73 (63– 82)	0.814
BMI, Mean (SD)	24.4 (5.4)	24.7 (4.8)	24 (6)	0.432
BMI of more than 30 kg/m²	16 (8.8%)	9 (11.7%)	7 (6.7%)	0.239
Number of COVID-19 vaccination injections*				
No injection	27 (14.8%)	5 (6.5%)	22 (21.0%)	0.007
1 injection	4 (2.2%)	2 (2.6%)	2 (1.9%)	0.916
2 injections	35 (19.2%)	13 (16.9%)	22 (21.0%)	0.491
3 injections	96 (52.7%)	50 (64.9%)	46 (43.8%)	0.005
4 injections	15 (8.2%)	7 (9.1%)	8 (7.6%)	0.721
No data	5 (2.7%)	0	5 (4.8%)	N/A
Number of COVID-19 mRNA vaccination injections				
No injection	59 (32.4%)	19 (24.7%)	40 (38.1%)	0.036
1 injection	96 (52.7%)	47 (61.0%)	49 (46.7%)	0.097
2 injections	20 (11.0%)	9 (11.7%)	11 (10.5%)	0.867
3 injections	3 (1.7%)	2 (2.6%)	1 (1.0%)	0.409
4 injections	0 (0.0%)	0 (0.0%)	0 (0.0%)	N/A
No data	4 (2.2%)	0 (0.0%)	4 (2.2%)	N/A
Comorbidities	159 (87.4%)	63 (81.8%)	96 (91.4%)	0.071
Hypertension	73 (45.9%)	31(49.2%)	42 (43.8%)	0.986
Diabetes mellitus	62 (39.0%)	27 (42.9%)	35 (36.5%)	0.843
Dyslipidemia	54 (34.0%)	25 (39.7%)	29 (30.2%)	0.505
Coronary artery diseases	46 (28.9%)	18 (28.6%)	28 (29.2%)	0.588
Immunodeficiency	31 (19.5%)	8 (12.7%)	23 (24.0%)	0.041
Chronic renal disease	27 (17.0%)	3 (4.8%)	24 (25.0%)	< 0.001
Cancer	18 (11.3%)	7 (11.1%)	11 (11.5%)	0.741
Pulmonary diseases	16 (10.1%)	5 (7.9%)	11 (11.5%)	0.339
Liver disease	9 (5.7%)	2 (3.2%)	7 (7.3%)	0.305
Autoimmune diseases	7 (4.4%)	0	7 (7.3%)	0.021
HIV	2 (1.3%)	0	2 (2.1%)	0.508
Pneumonia	47 (25.8%)	17 (22.1%)	30 (28.6%)	0.323
Remdesivir duration of hospitalization, mean (SD, days)	6.7 (5.7)	N/A	6.7 (5.7)	N/A

*Include vaccine, inactivated vaccine (Sinovac, Sinopharm); viral vector (AstraZeneca); and mRNA (Moderna or Pfizer BioNTech); IQR, interquartile range; BMI, body mass index; SD, standard deviation; mRNA, messenger RNA; N/A, no data; HIV, human immunodeficiency virus; N/A, no data.

There was no difference in the clinical severity between the molnupiravir and remdesivir groups. The overall treatment failure was 16.5%, and there was a significant difference in the treatment failure rate between the remdesivir and molnupiravir groups (22.9% *vs.* 7.8%; $P = 0.007$). Twenty-four patients who received remdesivir with treatment failure had extended remdesivir treatment from 3 to 5 days. For patients receiving molnupiravir, treatment failure occurred in six cases, who changed their treatment regimen from molnupiravir to remdesivir. There were no deaths or rehospitalizations within 30 days after antiviral therapy in either group. Data are shown in **Table 3**.

Factors associated with treatment failure in patients with COVID-19 who received molnupiravir or remdesivir are shown in **Table 4.** From univariate analysis, male gender (OR = 3.1), number of COVID-19 vaccines (OR = 0.7), and pneumonia (OR = 2.7) were associated with treatment failure with statistical significance. From multivariate analysis, male gender (aOR = 3.4) and pneumonia (aOR = 2.5) were associated with treatment failure with statistical significance.

More patients in the molnupiravir group complained of ADRs. Furthermore, headache or dizziness (3.8%) and diarrhea (5.2%) were the leading ADRs of remdesivir and molnupiravir, respectively. The data on ADRs of molnupiravir and remdesivir are shown in **Table 5**. In the molnupiravir group with 77 patients, there were two cases of noncompliance. One participant missed taking the medication on two occasions, and the other participant took the medication only once daily until Day 4.

Table 3. Clinical severity and treatment outcomes in mild-moderate COVID-19 patients receiving molnupiravir or remdesivir.

Characters, n (%)	Total (n = 182)	Molnupiravir (n =77)	Remdesivir (n = 105)	*P*-value
Clinical severity				
Mild	135 (74.2%)	60 (77.9%)	75 (71.4%)	0.323
Treatment outcomes				
Clinical resolved by day 5	44 (24.2%)	9 (11.7%)	35 (33.3%)	< 0.001
Clinical resolved by day 10	105 (57.7%)	30 (39.0%)	75 (71.4%)	< 0.001
Treatment failure	30 (16.5%)	6 (7.8%)	24 (22.9%)	0.007
Rehospitalization within 30 days	0	0	0	N/A
Switching the regimen from molnupiravir to remdesivir	6 (3.3%)	6 (7.8%)	N/A	N/A
Extending the duration of remdesivir	27 (14.8%)	3 (3.9%)	24 (22.9%)	0.014

N/A, no data

Table 4. Factors associated with treatment failure in mild-moderate COVID-19 patients receiving molnupiravir or remdesivir.

Factors	Univariate analysis			Multivariate analysis		
	OR	95%CI	*P*-value	aOR	95%CI	*P*-value
Male	3.1	1.4– 6.7	**0.005**	3.4	1.5– 7.8	**0.004**
Age	1.0	1.0–1.1	0.067	-	-	-
Number of COVID-19 vaccine	0.7	0.5–1.0	**0.030**	0.7	0.5– 1.0	0.064
Pneumonia	2.7	1.2–5.8	**0.012**	2.5	1.1– 5.8	**0.032**
Diabetes mellitus	0.8	0.3–1.9	0.591	-	-	-
Coronary artery diseases	1.3	0.6–3.1	0.529	-	-	-
Immunodeficiency	1.6	0.6–4.2	0.319	-	-	-
Chronic renal disease	0.6	0.2–2.1	0.412	-	-	-
Cancer	2.1	0.7–6.5	0.186	-	-	-
Pulmonary diseases	1.2	0.3–4.4	0.807	-	-	-

aOR, adjusted odds ratio; CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio.

Table 5. Molnupiravir and remdesivir adverse drug reactions.

Adverse drug reactions	Molnupiravir (n = 77)	Remdesivir (n = 105)
Nausea and vomiting	2 (2.6 %)	2 (1.9%)
Headache or dizziness	2 (2.6%)	4 (3.8%)
Eye edema	1 (1.3%)	0 (0.0%)
Diarrhea	4 (5.2%)	0 (0.0%)
Rash	2 (2.6%)	0 (0.0%)
Taste abnormality	1 (1.3%)	0 (0.0%)
Constipation	0 (0.0%)	1 (1.0%)
Shaking	0 (0.0%)	1 (1.0%)
Bradycardia	0 (0.0%)	0 (0.0%)
Total	**12 (15.6%)**	**8 (7.6%)**

Discussion

Our study showed a significant difference in the treatment failure rates of patients with mild-to-moderate COVID-19 who were treated with remdesivir for three days compared to those treated with molnupiravir. It was observed that the remdesivir group had patients with a higher risk of developing severe symptoms than the molnupiravir group. Moreover, patients in the remdesivir group had significantly more comorbidities and fewer vaccinations. Physicians may extend the duration of remdesivir treatment among these patients. We found that patients received an extension of remdesivir treatment from 3 to 5 days in the remdesivir group. Our results differ from those in a study conducted in Italy, which studied the treatment outcome in patients with COVID-19 who received molnupiravir, remdesivir, or nirmatrelvir/ritonavir as outpatients. They found no significant difference in treatment outcomes between patients who received molnupiravir (1.8%) and remdesivir (5.1%), but significant differences between those who were treated with nirmatrelvir/ritonavir and remdesivir.[9] More patients in the remdesivir group from that study had a higher median age and immunosuppressive status than those who received molnupiravir and nirmatrelvir/ritonavir, which was similar to our study.[9] Another real-world study in Italy involved patients with a confirmed diagnosis of SARS-CoV-2 through a positive nasopharyngeal swab. Nonhospitalized patients with mild-to-moderate COVID-19 disease and one or more risk factors for progression to severe illness were considered for early treatment. Their result revealed similar composite endpoints (pneumonia, acute respiratory distress syndrome, COVID-19, and non-COVID-19-related death) in patients receiving molnupiravir (2.8%), remdesivir (3.0%), and nirmatrelvir/ritonavir (1.3%).[10] The clinical resolution by day 5 and day 10 was higher in patients receiving remdesivir compared to those receiving molnupiravir. This difference may be attributed to the fact that patients treated with remdesivir were admitted to hospital, where they received close monitoring of their clinical responses and prompt management of any issues. In addition, compliance with medication treatment may have been better in the remdesivir group than in the molnupiravir group. Our study identified two non-compliance patients in the molnupiravir group. These factors could have contributed to the better clinical outcomes observed by day 5 and day 10. Our study did not observe any deaths or rehospitalizations within 30 days after antiviral therapy in either of the molnupiravir or remdesivir groups. A possible explanation is that only a quarter of all patients with moderate COVID-19 severity were included, and vaccination status could alleviate the course of the Omicron COVID-19 strain. From our study results, we found that most patients in the treatment failure group had extended remdesivir treatment from 3 days to 5 days. Extending remdesivir treatment might have mortality and rehospitalization benefits in some cases. Close monitoring of the signs and symptoms of patients with COVID-19 is required. In a previous randomized study that compared three days of remdesivir with a placebo in symptomatic, nonhospitalized patients with COVID-19 who were at high risk for disease progression, COVID-19-related hospitalization or death from any cause occurred in two patients (0.7%) in the remdesivir group; however, no patients had died by Day 28, which was similar to our study.[4] A systematic review and meta-analysis in adult patients with the Omicron variant of COVID-19 and mild-to-moderate severity revealed that the risk of mortality was reduced by 34.0%, and the risk of the composite

outcome of disease progression was reduced by 37.0% among patients who received molnupiravir compared to those who received the placebo.[11] Another randomized study evaluated the efficacy and safety of treatment with molnupiravir in nonhospitalized, unvaccinated patients with mild-to-moderate COVID-19. The result showed that one death was reported in the molnupuravir group, and 7.3% of patients died from any cause or were hospitalized through day 29, which was higher than our result.[12] Therefore, close monitoring of the signs and symptoms of patients with COVID-19 is still required for better outcomes.

Several factors could contribute to the poor treatment outcomes and disease progression during hospitalized COVID-19 infection, such as age ≥55 years, chronic obstructive pulmonary disease, chronic kidney disease, asthma, diabetes mellitus, HIV/AIDS, worsening conditions, history of smoking, respiratory failure, albumin, and c-reactive protein.[13, 14] Another study from Italy revealed that three or more comorbidities, hematological disease, gastrointestinal symptoms, time from symptom onset to antiviral treatment and each-day increment were associated with death or hospitalization due to COVID-19.[9] In our study, factors that contributed to treatment failure from univariate analysis were the number of COVID-19 vaccines, male gender, and pneumonia. This emphasized the benefit of the COVID-19 vaccine on the patient's treatment outcome. Furthermore, a large retrospective study in Hong Kong in patients with confirmed COVID-19 showed that those who had received ≥ 3 doses of CoronaVac or ≥ 2 doses of Comirnaty vaccines had a greater survival rate than those who were unvaccinated. For patients aged ≥ 60 years, receipt of CoronaVac or Comirnaty vaccines was associated with lower risks for all-cause mortality and progression to a serious condition.[15] Thus, we recommend close monitoring of patients with COVID-19 and pneumonia.

A few patients from our study had ADRs. Diarrhea was the most common ADR for molnupiravir, which is similar to a previous study.[9] Headaches or dizziness were the most common ADRs for remdesivir, which was different from a previous study.[4] While nausea and headache were widely mentioned in an earlier study, they were rarely reported in this study.[4] Furthermore, bradycardia is another ADR that has been reported for remdesivir.[9] There may be an underreporting of bradycardia symptoms from patients included in our study. In addition, a recall bias for nausea, which was a minor symptom, might have affected the ADR result. However, these results may imply that molnupiravir and remdesivir are safe medications and that there is no need for close monitoring. The graphical abstract is illustrated in **Figure 2.**

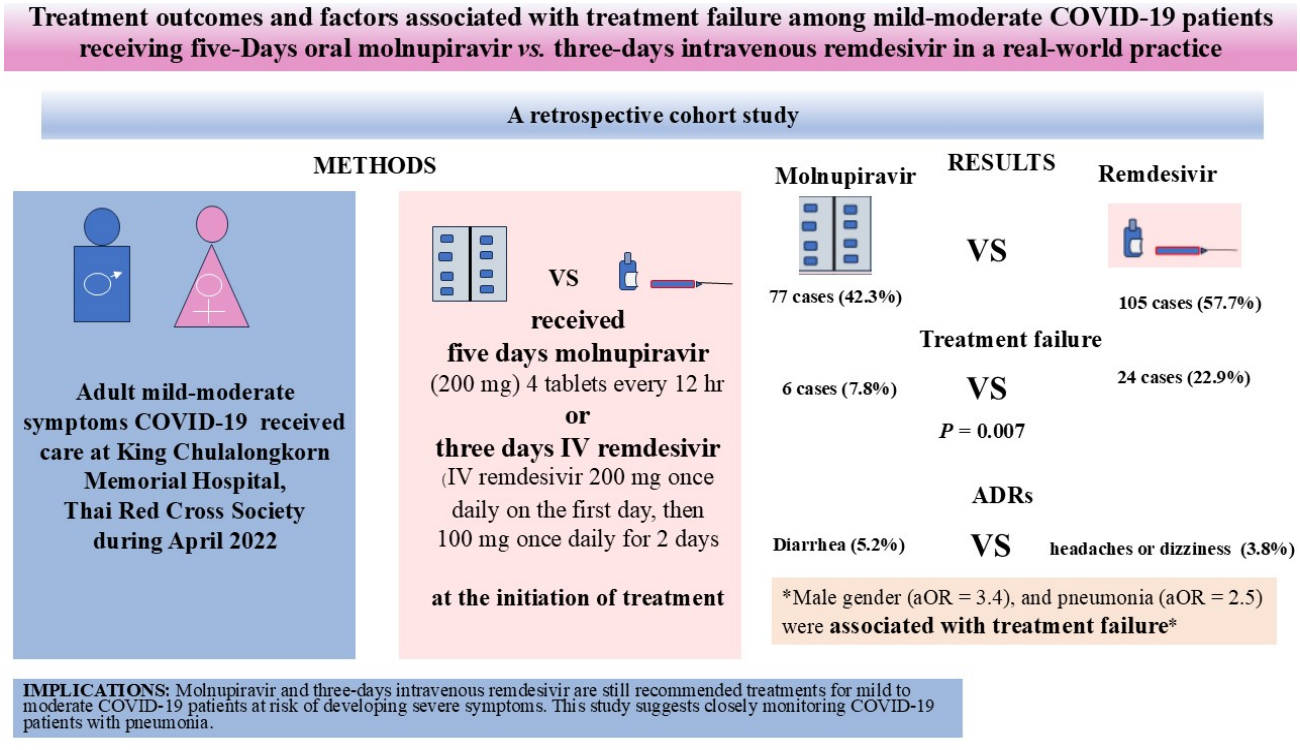

Figure 2. Graphical abstract illustrates the key concept and findings of this study.

The selection of antiviral therapy for COVID-19 is based on several factors, such as COVID-19 severity, comorbidities, drug interactions, gastrointestinal absorption, safety, adherence, and pregnancy status. Molnupiravir is an oral drug that is easy to administer, and no dosage adjustment is required for patients with decreased renal function, but it is not authorized for use in patients under 18 years, and it is not recommended for pregnant women. Moreover, it has no known major interactions with other drugs and has few ADRs. It can be administered without the patient needing to alter their normal food consumption routines.[3, 16] For a three-day regimen of remdesivir, the drug is administered intravenously once daily for three consecutive days. The injection, which is suitable for outpatient settings, can be given to pregnant women or patients who cannot take oral medication.[3, 17] We cannot conclude that molnupiravir is more effective than the three-day remdesivir regimen because our retrospective data revealed different characteristics between the molnupiravir and remdesivir groups, such as age, number of COVID-19 vaccinations, and comorbidities. The small number of patients at a single center and the short time for data collection may restrict the generalizability of our results. Even though the IDSA treatment guidelines for COVID-19 recommend nirmatrelvir/ritonavir as the preferred therapy for nonhospitalized patients with COVID-19 and a high risk of progression to severe COVID-19, nirmatrelvir/ritonavir has several drug interactions.[3, 18] Healthcare professionals have to assess drug–drug interactions before prescribing nirmatrelvir/ritonavir. In this instance, molnupiravir or three days of remdesivir may be an alternative option.

Our study had some strengths and limitations. This study demonstrated the treatment outcomes and ADRs in real-life practice. In addition, we conducted the study during the period when the Omicron variant of COVID-19 was prevalent and in the era of complete vaccination. Therefore, we can apply our results to the current COVID-19 situation. We also evaluated the factors associated with treatment failure in patients with COVID-19 that could encourage policymakers to provide appropriate vaccines and medications in different countries. However, our study was conducted when nirmatrelvir/ritonavir was unavailable in Thailand; therefore, real-world practices might be redesigned with future studies. There might be some recall bias in our ADR data. Our study collected data from a single center with a small sample size. The retrospective nature of the study resulted in missing data and an imbalance in the baseline characteristics between the two groups, such as comorbidities, the onset of illness, and vaccination status, which may have affected the clinical outcomes. Another factor that may have influenced treatment outcomes is hospitalization status. Patients receiving remdesivir were hospitalized, while those receiving molnupiravir were treated as outpatients in this study. This was not evaluated in association with treatment failure, and it may have influenced the clinical outcomes between the two groups. Future research is required with a larger population, through multi-center approaches, and with a prospective study design.

Conclusion

Choosing an antiviral agent for the treatment of COVID-19 depends on drug availability, the patient's condition, and hospital policy. Molnupiravir and three days of remdesivir are still the recommended antiviral drugs for patients with mild-to-moderate COVID-19 and risk factors of disease progression with very low ADRs. However, our study suggests the close monitoring of patients with COVID-19 and pneumonia, as well as unvaccinated or incompletely vaccinated patients. These patients might develop treatment failure and require extended treatment with antiviral agents or hospitalization.

Acknowledgements

We would like to thank the physicians, nurses, pharmacists, and other healthcare professionals at King Chulalongkorn Memorial Hospital for their devotion to taking care of patients with COVID-19 during the pandemic. Furthermore, we would like to thank Pharm D students and infectious disease pharmacy residents from the Faculty of Pharmaceutical Sciences, Chulalongkorn University, for following up on the patients with COVID-19 by phone.

Conflict of interest statement

None of the authors discloses any potential conflict of interest.

Data sharing statement

All data generated or analyzed in the present study are included in the published article. Further details are available for non-commercial purposes from the corresponding author upon reasonable request.

References

1. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol 2021;19: 141–54.
2. Singh M, de Wit E. Antiviral agents for the treatment of COVID-19: progress and challenges. Cell Rep Med 2022;3:100549.
3. Bhimraj A, Morgan RL, Shumaker AH, Baden LR, Cheng VC-C, Edwards KM, et al. Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19 (September 2022). Clin Infect Dis 2022;78:e250–e349.
4. Gottlieb RL, Vaca CE, Paredes R, Mera J, Webb BJ, Perez G, et al. Early remdesivir to prevent progression to severe Covid-19 in outpatients. N Engl J Med 2022;386:305–15.
5. Goldman JD, Lye DCB, Hui DS, Marks KM, Bruno R, Montejano R, et al. Remdesivir for 5 or 10 days in patients with severe Covid-19. N Engl J Med 2020;383:1827–37.
6. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for the treatment of Covid-19 - final report. N Engl J Med 2020;383: 1813–26.
7. Lam C, Patel P. Nirmatrelvir-Ritonavir. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
8. World Health Organization. Living guidance for clinical management of COVID-19: Living guidance. Geneva: World Health Organization; 2021.
9. Tiseo G, Barbieri C, Galfo V, Occhineri S, Matucci T, Almerigogna F, et al. Efficacy and safety of nirmatrelvir/ritonavir, molnupiravir, and remdesivir in a real-world cohort of outpatients with COVID-19 at high risk of progression: The PISA outpatient clinic experience. Infect Dis Ther 2023;12:257–71.
10. Del Borgo C, Garattini S, Bortignon C, Carraro A, Di Trento D, Gasperin A, et al. Effectiveness, tolerability and prescribing choice of antiviral molecules molnupiravir, remdesivir and nirmatrelvir/r: a real-world comparison in the first ten months of use. Viruses 2023;15:1025.
11. Huang C, Lu TL, Lin L. Real-World clinical outcomes of molnupiravir for the treatment of mild to moderate COVID-19 in adult patients during the dominance of the omicron variant: a meta-analysis. Antibiotics (Basel) 2023;12:393.
12. Jayk Bernal A, Gomes da Silva MM, Musungaie DB, Kovalchuk E, Gonzalez A, Delos Reyes V, et al. Molnupiravir for oral treatment of Covid-19 in nonhospitalized patients. N Engl J Med 2022;386: 509–20.
13. Kaso AW, Hareru HE, Kaso T, Agero G. Factors associated with poor treatment outcome among hospitalized COVID-19 patients in South Central, Ethiopia. Biomed Res Int. 2022;2022:4551132.
14. Liu W, Tao Z-W, Wang L, Yuan M-L, Liu K, Zhou L, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chin Med J (Engl) 2020;133: 1032–8.
15. Cheung YYH, Lau EHY, Yin G, Lin Y, Cowling BJ, Lam KF. Effectiveness of vaccines and antiviral drugs in preventing severe and fatal COVID-19, Hong Kong. Emerg Infect Dis 2024;30:70—8.
16. Maas BM, Strizki J, Miller RR, Kumar S, Brown M, Johnson MG, et al. Molnupiravir: mechanism of action, clinical, and translational science. Clin Transl Sci 2024;17:e13732.
17. Aleem A, Kothadia JP. Remdesivir. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
18. Marzolini C, Kuritzkes DR, Marra F, Boyle A, Gibbons S, Flexner C, et al. Recommendations for the management of drug-drug interactions between the COVID-19 antiviral nirmatrelvir/ritonavir (Paxlovid) and comedications. Clin Pharmacol Ther 2022;112: 1191–200.