OPEN ACCESS Freely available online

Journal of Clinical Toxicology

Research Article

Efficacy and Tolerability of Sotrovimab, Molnupiravir, and Nirmatrelvir/Ritonavir for Non-Hospitalized Patients at High Risk for COVID-19: A Retrospective, Single-Center Analysis

Victoria Kauer[1*], David Totschnig[1], Max Augustin[2], Ferdinand Waldenberger[3,4], Mario Karoly[1], Michelle Nägeli[1], Christoph Wenisch[1]

[1]Department of Medicine, Klinik Favoriten, Vienna Healthcare Group, Kundratstraße 3, 1100 Vienna, Austria; [2]Department of Internal Medicine, University Hospital Cologne, 50937 Cologne, Germany; [3]Department of Medicine, Sigmund Freud University, Vienna, Austria; [4]Department of Medicine, Samariterbund, University of Vienna, Vienna, Austria

ABSTRACT

Background: The use of outpatient antiviral treatment for high-risk patients with coronavirus disease 19 (COVID-19) is crucial in preventing the progression to severe COVID-19 and reducing hospitalization rates.

Objective: The main goal of this retrospective, single-center analysis was to assess the feasibility and potential clinical impact of an outpatient administration of various available antiviral agents including Sotrovimab (SOT), Nirmatrelvir/Ritonavir (N/R), and Molnupiravir (MOL) to COVID-19 patients at high risk for disease progression. In addition, hospital admission rates between groups, side effects and subjective treatment effects were assessed.

Methods: We conducted a retrospective analysis on 2606 outpatient individuals with mild to moderate COVID-19 at risk for disease progression, hospitalization, or death. After receiving either SOT (420/2606), MOL (1788/2606), or N/R (398/2606), patients were followed-up regarding primary (hospitalization rate) and secondary (treatment and side effects) outcomes by phone.

Result: A total of 2606 patients were treated at the outpatient clinic, of whom 420 were treated with SOT, 398 with N/R, and 1788 with MOL. 10 patients (3.2%) who were treated with SOT were later hospitalized and 1 patient had to be admitted to the ICU. In comparison, 11 patients (0.8%) who received MOL were admitted to the hospital (2 admissions to the Intensive Care Unit (ICU). No hospital/ICU admission was registered for patients who received N/R. In contrast, 46 patients (14.3%) who received N/R reported strong to severe side effects, exceeding SOT with 2.6% of the patients (8 patients in total) and MOL with 5% (69 patients) reporting strong to severe side effects. A reduction in COVID symptoms after the medication administration was experienced by 43% (132 patients) in the SOT group, 43% (572 patients) in the MOL group, and 67% (115 patients) in the N/R group, respectively. In over 60-year-olds and chronic kidney disease, no subjective symptom improvement is to be expected with MOL. Women have a 1.2 elevated chance of symptom improvement with treatment with MOL.

Conclusion: Hospitalization rates in high-risk patients who received SOT, MOL, or N/R were low, particularly in patients who received N/R. All antiviral drugs were well tolerated, but side effects were more frequent in patients with N/R. However, N/R showed the greatest subjective treatment effect.

Keywords: COVID-19; Antiviral drugs; Sotrovimab; Molnupiravir; Side effects

Correspondence to: Victoria Kauer, Department of Medicine, Klinik Favoriten, Vienna Healthcare Group, Kundratstraße 3, 1100 Vienna, Austria, E-mail: victoria.kauer@gmx.at

Received: 21-Apr-2023, Manuscript No. JCT-23-23685; **Editor assigned:** 24-Apr-2023, PreQC No. JCT-23-23685 (PQ); **Reviewed:** 08-May-2023, QC No. JCT-23-23685; **Revised:** 15-May-2023, Manuscript No. JCT-23-23685 (R); **Published:** 22-May-2023, DOI: 10.35248/2161-0495.23.13.544.

Citation: Kauer V, Totschnig D, Augustin M, Waldenberger F, Karoly M, Nägeli M, et al (2023) Efficacy and Tolerability of Sotrovimab, Molnupiravir, and Nirmatrelvir/Ritonavir for Non-Hospitalized Patients at High Risk for COVID-19: A Retrospective, Single-Center Analysis. J Clin Toxicol. 13:544.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic rapidly spread across the globe, even among communities with a high level of preexisting immunity due to vaccination [1-4]. Efficient and safe antivirals are vital to treat Severe Acute Respiratory Syndrome Coronavirus type 2 (SARS-COV-2)-related infections as early as possible in an outpatient setting to prevent disease progression and thus hospitalization and death [5]. Sotrovimab (SOT), Molnupiravir (MOL), and Nirmatrelvir/Ritonavir (N/R) have been shown to reduce the risk of hospitalization and COVID-19-related death. The start of all three drugs is recommended as early as possible after infection, but at the latest within the first five days after the onset of symptoms [6,7].

Nirmatrelvir/ritonavir is an approved SARS-CoV-2 protease inhibitor containing the active component nirmatrelvir and ritonavir, a pharmaceutical enhancer [8]. It has been granted Emergency Use Authorization (EUA) in December 2021 as therapy for non-hospitalized patients (adults and children of twelve years and older) [9]. Sotrovimab is a monoclonal antibody, administered in form of a one-time intravenous infusion, directed against the SARS-CoV-2 virus by binding the virus's spike protein [10]. Nirmatrelvir/ritonavir and SOT have been approved for patients with COVID-19 without the need for oxygen supplementation who are at high risk for progression to severe disease. Molnupiravir acts as an orally active RdRp (RNA-dependent RNA polymerase) inhibitor to reduce viral load and has not yet been approved for use in the European Union and the United States [6,7,11]. Here, a retrospective single-center analysis was performed to provide real-world data on the efficacy and safety of Sotrovimab (SOT), Molnupiravir (MOL), and Nirmatrelvir/Ritonavir (N/R) in preventing severe COVID-19 outcomes during the Delta and Omicron surge in Vienna, Austria.

MATERIALS AND METHODS

Study design and outcomes

This retrospective analysis was based on data obtained by the Vienna health authorities which receive electronic laboratory reports on all patients who test positive for SARS-CoV2 in Vienna. The study included data from patients who were recently diagnosed with SARS-CoV2 infection and deemed at high risk for severe COVID-19 and thus invited for outpatient antiviral treatment between January 2nd, 2022, and June 29th, 2022. The prevailing variants of the SARS-CoV-2 virus were Delta (B.1.617.2) between December 2021 and January 2022, Omicron (BA.1.) from mid-January to March, Omicron (BA.2) from March to May 2022 and Omicron (BA.4/5) from May onwards. The primary study outcome was hospitalization due to COVID-19. The secondary study outcomes were the subjective effect of the different drugs, as well as treatment-associated side effects.

Study population

Following a positive SARS-CoV-2 swab and electronic reporting by the laboratories, patients were contacted by telephone by the health authorities of Vienna, and those who were at high risk for disease progression, hospitalization, or death were offered outpatient per oral (N/R or MOL) or intravenous (SOT) antiviral treatment, respectively. The study population comprised individuals who had (1) Confirmed SARS-CoV-2 infections, (2) Received a diagnosis of COVID-19 as outpatients, (3) Were assessed as being at high risk for progression to severe disease, (4) Suffered from mild-to-moderate symptoms and (5) Were deemed eligible to receive antiviral therapy. High-risk patients were identified based on a risk model that was developed in accordance with NIG (National Immunization Board) to evaluate the risk of severe COVID-19 in patients infected with SARS-CoV-2. Prioritization of the risk groups was based on the presence of one of four key elements: (1) Older age, (2) No receipt of previous SARS-CoV2 vaccination, (3) Immunosuppression, and (4) Clinical risk factors. The most common risk factors were (1) Age>50 years, (2) Obesity (BMI>30), (3) Cardiovascular diseases, (4) Diabetes mellitus, (5) Chronic lung and respiratory diseases, (6) Chronic kidney diseases with impairment of the kidney function, (7) Chronic liver disease with impaired liver function, (8) Chronic psychiatric disorders and/ or (9) Chronic neurological diseases.

Drug allocation was performed according to eligibility and availability criteria as well as the patient's preference through telemedicine by a physician. Oral medication, as in MOL and N/R, was delivered to the patients' homes. Intravenous SOT was administered at a dedicated infusion ward at the hospital (Klinik Favoriten). Eligibility criteria for the individual drugs were also dependent on supply and demand changes. For this outpatient program, sotrovimab was available from January 3rd, 2022, while MOL was available from the 28th of January 2022 and N/R was only available from the 15th of March 2022 onwards until the end of the analyzed time span. In order of preference, the following therapeutics were recommended based on availability: 1. N/R, 2. SOT, 3. MOL.

For each patient, a questionnaire-based Follow-Up (FU) interview was conducted after 28 days *via* telemedicine. This FU had the intention to assess the effect of the therapy forms, as well as the prevalence of adverse reactions and serious adverse events. In a set of 12 questions, patients were asked about (1) Symptom start, (2) Date of first positive and (3) First new negative SARS-CoV-2 PCR Test, (4) Hospital administration and/or (5) COVID-19-related admission to the Intensive Care Unit (ICU), (6) Side effects they noticed during treatment and (7) Their subjective well-being after drug administration. In addition, other questions mentioned included (8) Adherence to medication, (9) Allergic reactions to the medication, and (10) Drug interactions with other medication. Concerning the subjective therapeutic effect, patients were asked (11) whether the treatment showed a good, moderate, or no effect, by subjectively rating the alleviation or worsening of symptoms during treatment. Finally, patients were asked (12) To rate the side effects on a scale of one to four (1: Severe side effects, 2: Moderate 3: Mild, 4: No side effects).

Statistical analysis

Data were analyzed using GraphPad Prism 9 (Dotmatics, Boston, MA, USA) and SPSS (IBM 23, USA). P-values of 0.05 and lower

were considered scientifically significant. All values are represented as the median with Interquartile Range (IQR), unless otherwise stated. The results from the outcomes are represented as % (n/N), with N representing the patients with a complete follow up for the corresponding question, not the patient number in total. In the MOL cohort, binomial regression models for subjective symptom improvement according to the presence or absence of risk factors such as older age, pre-existing conditions, and sex were performed. Here, unadjusted risk ratios with 95% Confidence Intervals (CI), as well as Chi-square tests were calculated. STATA version 17.0 and GraphPad Prism (GraphPad Software, La Jolla, CA) were used to compile the analyses and graph the data.

RESULTS

Data from a total of 2606 patients was included in the analysis. The median age was 62 years (Interquartile Range (IQR) 18-101); 42% (1096/2606) were 65 years of age or older and 47% (1219/2606) were women. Age ranged from 18 to 101 years old. Among the 2606 patients in the study cohort, 15%(398/2606) received at least one dose of N/R, while 16%(420/2606) received SOT and 68% (1788/2606) were treated with MOL during the study period. Considering the different treatment arms, age, gender, and risk factors did not show significant variations. Risk factors for severe illness were only collected in patients who received MOL. The most common risk factors in this patient collective included age over 50 years (58%), followed by cardiovascular diseases (17%), Body Mass Index (BMI)>30 (10%), Diabetes Mellitus type 2 (7%) and chronic renal disease (2.7%) (Table 1).

Hospitalization rates were low in all three treatment arms. In the SOT group, 3.2% (10/420) of patients were later admitted to the hospital. 0.32% (1/309) were admitted to the ICU. In comparison, 0.8% (11/1406) of the patients who received MOL were admitted to the hospital, and 0.1% (1/1406) were admitted to the ICU. No patient who received N/R was admitted to the hospital (0/333). In the MOL group, four patients were hospitalized due to COVID-related respiratory failure, two patients due to hypertension, four patients due to gastrointestinal symptoms, and one patient due to fatigue symptoms. In the SOT group, most patients were hospitalized due to hypotension and fatigue symptoms. Additionally, two patients were hospitalized due to a hypotensive reaction directly after SOT administration.

43% (132/309) of the patients who received SOT experienced a good treatment effect after treatment, 30% (93/309) experienced a moderate treatment effect and 27% (84/309) experienced no effect. 43% (572/1334) of the patients who received MOL experienced a good treatment effect during treatment, while 29% (388/1334) experienced a moderate and 28% (374/1334) experienced no treatment effect. 67%(115/227) of the patients who received N/R reported a good treatment effect, while 23% (39/227) experienced a moderate treatment effect, and 10% (17/1334) of the patients reported no subjective treatment effect.

Regarding the group of patients, that received SOT most patients 85% (263/309) did not show any new symptoms after drug administration, while 15% (46/ 309) did show new symptoms, out of which 0.003% (1/309) were self-reported to be severe, as in reduced responsiveness, resulting in hospital

Characteristic	MOL (n=1788)	N/R (n=398)	SOT (n=420)	Total (n=2606)
Female Sex-no. (%)	949 (53)	219 (55)	219 (52)	1387 (53)
Age group-no. (%)				
18-49 years	18 (4%)	48 (12%)	18 (4%)	171 (7%)
>50 years	402 (96%)	350 (88%)	402 (96%)	2435 (93%)
Median age (IQR)-y	61 (18-101)	62 (18-97)	64 (21-101)	62 (18-101)
Risk factors for severe illness-no. (%)				
BMI>30	167 (10)	N.A.	N.A.	N.A.
Cerebrovascular disease	23 (1)	N.A.	N.A.	N.A.
Cardiovascular disease	280 (17)	N.A.	N.A.	N.A.
Diabetes mellitus Type II	117 (7)	N.A.	N.A.	N.A.
Chronic renal disease	47 (3)	N.A.	N.A.	N.A.
Chronic liver disease	24 (1)	N.A.	N.A.	N.A.
Immunocompromised patients	28 (1)	N.A.	N.A.	N.A.
Malignancies	36 (1)	N.A.	N.A.	N.A.

Note: MOL: Molnupiravir; N/R: Nirmatrelvir/Ritonavir; SOT: Sotrovimab; no: Number; y: Years; BMI: Body Mass Index; N.A.: Not Available.

Table 1: Demographics and patient characteristics.

admission. New symptoms mostly included nausea, circulatory collapse, hypotension, vertigo, headaches, shivers, and rare cases of exanthema. One serious adverse event of atrial fibrillation occurred.

Regarding the N/R patient collective, 46.6% (150) of the patients self-reported new symptoms after treatment, including 3.7% (12/322) of the patients having experienced severe new symptoms. 53.4% (172/322) of the patients did not show any new symptoms at all. Recurrently mentioned symptoms included mostly gastrointestinal symptoms, foremost diarrhea, dysgeusia (metallic, bitter taste), hypertension, exanthema, circulatory problems, and headaches.

78% (1048/1349) of the patients in the MOL patient collective showed no new symptoms after treatment administration. In comparison, 22% (301/1349) of the patients showed new symptoms including 7% (23/1349) who self-reported severe new symptoms. Reported symptoms comprised gastrointestinal complaints (abdominal cramps, diarrhea, vomiting), blood hypertension, headaches, exanthema, itching, circulatory complaints, and vertigo. 300/1788 patients submitted a detailed description of experienced side effects. 56/300 did not experience any side effects, proportional allocation of new symptoms after MOL administration of 244/300 patients is presented in Table 2.

Secondary outcome: Risk stratification for MOL

The different risk factors that led to treatment recommendations were only assessed for patients who received MOL. Risk stratification for this patient collective showed that women had a 1, 2 (OR 1.0-1.5, p=0.04) higher chance of a subjective treatment effect than men. Patients over the age of 60 and patients with chronic kidney disease were less likely to report symptom improvement after starting MOL, although this did not reach statistical significance (Table 3).

Symptoms	
Diarrhea	59 (24%)
Nausea	52 (21%)
Headache	40 (16%)
Abdominal pain	37 (15%)
Exanthema	33 (14%)
Dizziness	31 (13%)
Fatigue	12 (5%)
Pruritus	8 (3%)
Elevated blood pressure	8 (3%)
Coughing	5 (2%)
Shortness of breath	3 (1%)
Obstipation	2 (1%)
Fever	1 (0.5%)

Table 2: New symptoms after MOL administration.

	Risk factors for symptom improvement	
	RR (95% CI	p-value
female sex	1.2 (1.0-1.5)	0.04
age >50	0.98 (0.82-1.2)	0.82
age >60	0.8 (0.67-0.96)	0.08
BMI >30	1.2 (0.91-1.6)	0.19
Cerebrovascular disease	1.3 (0.6-2.2)	0.54
Chronic liver disease	1.3 (0.6-2.2)	0.72
Chronic kidney disease	0.41 (0.16-0.96)	0.05
Diabetes mellitus type 2	1.0 (0.71-1.5)	0.86
Immunosuppressive therapy	1.2 (0.6-2.1)	0.59
Cardiovascular disease	1.0 (0.79-1.3)	0.92
Cancer	1.1 (0.56-1.8)	0.85

Table 3: Risk factors for subjective symptom improvement.

DISCUSSION

In this retrospective single-center analysis of high-risk COVID-19 patients with mild to moderate symptoms not requiring hospitalization, outpatient therapy with single-dose Sotrovimab (SOT), or 5 days of Molnupiravir (MOL) or Nirmatrelvir/ Ritonavir (N/R) resulted in an overall low risk of disease progression and hospitalization. Patients who received SOT had the highest hospitalization rate with 3.2% (ICU administration of 0.3%), compared to 0.8% in the MOL collective (0.1% ICU admission). None of the patients, who received N/R were admitted to the hospital. Based on this limited data on the safety and efficacy of oral antiviral drugs, as well as SOT in patients with COVID-19, current guidelines and the medical community of Austria are now prioritizing their distribution to those who do not require supplemental oxygen but who are at the highest risk of disease progression. The analyzed study cohort reflected such a prescription pattern in real-world and the use of antiviral COVID-19 medication was clearly associated with a risk reduction in disease progression, reflected by low hospitalization rates for all three treatment options, but especially for nirmatrelvir/ ritonavir.

These findings are in line with other studies. The MOVe-OUT trial by Bernal, et al. [12], included 1433 participants and indicated a lower risk of hospitalization for any cause or death until day 29 in patients receiving MOL (28 of 385 participants (7.3%) versus placebo (53 of 377 (4.1%)). Similarly, SOT in non-hospitalized patients with mild to moderate COVID-19 caused by the Delta variant reduced all-cause hospitalization lasting longer than 24 hours or death (1% *vs.* placebo 6%) [13]. Another study by Wen et al. [3], showed that treatment with an antiviral drug (N/V, MOL) reduced hospitalization rates by approximately 80% when compared to a placebo.

The most common adverse events of the three oral antiviral drugs include nausea, abdominal pain and diarrhea, headache, vertigo, and circulatory complaints. In addition to these common side effects, patients who received N/R commonly reported a metallic taste, that lasted for hours, which previously has been shown to occur in around 5.6% of patients. [8]. A study by Hammond et al. [9], came to the results that dysgeusia and diarrhea occurred more often with N/R than with a placebo. The same study also indicates that N/R did neither improve nor aggravate the occurrence of adverse events, generally stating that this oral antiviral drug is safe [9].

In comparison to N/R (14.3%) the patients who received SOT reported significantly few new symptoms after drug administration (2.4%. However, some of the reported symptoms were self-classified to be of greater severity, such as circulatory collapse, hypotension, and nausea, which led to hospital admission in two cases. These results are in line with the placebo-controlled, randomized COMET-ICE study, in which the safety SOT was evaluated in 1,049 non-hospitalized COVID-19 patients, stating similar rates of adverse events in the placebo (19%) group and in the group having received SOT (17%). Serious adverse events, such as hypersensitivity and infusion-related reactions, as well as anaphylaxis, occurred in 2% of the patient collective (compared to 6% in the placebo group), but were considered not to be related to drug intake in all cases [14]. These results are in line with our results with most reported adverse events rather being linked to COVID-19 than to antiviral drugs.

Patients who took MOL reported strong to severe side effects in 5.1%, which is in line with other studies for example by Painter, et al. [11], stating that the occurrence of adverse events is low, and no significant difference can be found between the placebo group and the patient cohort. In this study mild to moderate adverse events were reported in 37.5%, showing comparable results to our analyzes, with similar rates of mild to moderate adverse events (42.9%). The most common side effects represented in the study were diarrhea, nausea, headache, and abdominal pain.

Experienced subjective treatment effects of the different treatments were difficult to quantify. Nonetheless, most patients who took N/R reported a beneficial treatment and alleviation of symptoms during therapy. This can be compared to a patient collective having received MOL with a good subjective treatment effect in 42% of the cases, which is like patients having been treated with SOT, who experienced alleviation in symptoms in 43% of the cases. Similar results are described in the EPIC-HR trial that showed that the efficacy of N/R was maintained in a population of participants at high risk for severe COVID-19, with N/R resulting in a risk of progression to severe COVID-19 that was 89% lower than the risk with placebo [9]. These results can be compared to the MOVe-OUT trial in which MOL was associated with a decrease in symptom progression and the relative risk of hospitalization by 30% [12]. The superiority of N/R in comparison to MOL was underpinned by a recent study by Burdet, et al. [15], in which the risk of all-cause mortality was reduced by 24% with MOL and by 66% with N/R. Nonetheless, a study comparing eight different studies suggests, that with moderate certainty evidence from these trials, MOL reduces the risk of hospital admission (43 fewer admissions per 1,000 patients at highest risk) and the time to symptom resolution (on average 3.4 fewer days), while low certainty evidence suggests a small effect on mortality (6 fewer deaths per 1,000 patients). Another retrospective study concluded that initiating N/R within the first 5 days of SARS-CoV-2 infection was associated with a significantly reduced risk of progression to severe COVID-19 or mortality [16].

Limitations to this study include the lack of a control group that did not receive any antivirals. Therefore, it can only be stated that hospitalization rates were overall low after the use of antiviral drugs, but efficacy could not be assessed versus no treatment. This would be of particular interest as the omicron VoC generally causes a milder clinical course as compared to former variants including alpha and delta which were predominant in most randomized trials concerning antiviral treatment. In addition, the clinical utility of monoclonal antibodies including SOT is severely limited by the emergence of some omicron subvariants showing a high degree of immune escape [2]. At the time of the study, BA.1 was the predominant strain in Vienna, for which SOT shows neutralization capability. A further limitation of our study is the heterogeneity of completed follow-ups in the different patient cohorts as well as

the different questions. No complete statements of the risk factors in the N/R and the SOT group were available; therefore this data was not included in the study.

CONCLUSION

Future placebo- controlled, large-sampled studies will be needed to assess the short-and long-term safety and efficacy of N/R, MOL, and SOT. Based on this retrospective single-center analysis providing real-world data, Sotrovimab (SOT), Molnupiravir (MOL), and Nirmatrelvir/Ritonavir (N/R) are feasible options for treating SARS-CoV-2 infected adults at risk for disease progression, hospitalization, or death in an outpatient setting. N/R showed the lowest hospitalization rate but was associated with over twice as many reported adverse events as compared to the other two treatments. MOL showed a low rate of adverse events, as well as a small percentage of hospitalized cases. SOT had the lowest rate of side effects but has to be given intravenously and efficacy varies in certain omicron subvariants. The safety and efficacy of the investigated drugs warrant further large-scale studies.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ETHICAL CONSIDERATIONS

The study was approved by the Institutional Review Board of the City of Vienna (EK 22-195-1022).

REFERENCES

1. Rivasi G, Bulgaresi M, Mossello E, Buscemi P, Lorini C, Balzi D, et al. Course and lethality of SARS-CoV-2 epidemic in nursing homes after vaccination in Florence. Vaccines. 2021;9(10):1174.
2. Takashita E, Yamayoshi S, Simon V, van Bakel H, Sordillo EM, Pekosz A, et al. Efficacy of antibodies and antiviral drugs against Omicron BA. 2.12. 1, BA. 4, and BA. 5 subvariants. N Engl J Med. 2022;387(5):468-470.
3. Wen W, Chen C, Tang J, Wang C, Zhou M, Cheng Y, et al. Efficacy and safety of three new oral antiviral treatment (molnupiravir, fluvoxamine and Paxlovid) for COVID-19 : A meta-analysis. Ann Med. 2022;54(1):516-523.
4. WHO. Coronavirus (COVID-19) data.
5. Imran M, Arora MK, Asdaq SM, Khan SA, Alaqel SI, Alshammari MK, et al. Discovery, development, and patent trends on molnupiravir: A prospective oral treatment for COVID-19. Molecules. 2021;26(19):5795.
6. FDA. Coronavirus (COVID-19) Update: FDA Authorizes additional oral antiviral for treatment of COVID-19 in certain adults. Food and Drug Administration. 2022.
7. Mahase E. Covid-19: Molnupiravir reduces risk of hospital admission or death by 50% in patients at risk, MSD Reports. 2021;375:n2422.
8. Pfizer Europe MA EEIG. Zusammenfassung der merkmale des arzneimittels. Pfizer Manufacturing Deutscchland GmBH. 2021.
9. Hammond J, Leister-Tebbe H, Gardner A, Abreu P, Bao W, Wisemandle W, et al. Oral nirmatrelvir for high-risk, nonhospitalized adults with Covid-19. NEJM. 2022;386(15):1397-1408.
10. Sotrovimab. Xevudy. European Medicines Agency (EMA). 2021.
11. Painter WP, Holman W, Bush JA, Almazedi F, Malik H, Eraut NC, et al. Human safety, tolerability, and pharmacokinetics of molnupiravir, a novel broad-spectrum oral antiviral agent with activity against SARS-CoV-2. Antimicrob Agents Chemother. 2021;65(5):e02428.
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(6): 509-520.
13. Huang DT, McCreary EK, Bariola JR, Minnier TE, Wadas RJ, Shovel JA, et al. Effectiveness of casirivimab-imdevimab and sotrovimab during a SARS-CoV-2 delta variant surge: A cohort study and randomized comparative effectiveness trial. JAMA Netw Open. 2022;5(7):e2220957.
14. Gupta A, Gonzalez-Rojas Y, Juarez E, Crespo Casal M, Moya J, Falci DR, et al. Early treatment for COVID-19 with SARS-CoV-2 neutralizing antibody sotrovimab. N Engl J Med. 2021;385(21): 1941-1950.
15. Burdet C, Ader F. Real-world effectiveness of oral antivirals for COVID-19. Lancet. 2022;400(10359):1175-1176.
16. Najjar-Debbiny R, Gronich N, Weber G, Khoury J, Amar M, Stein N, et al. Effectiveness of paxlovid in reducing severe coronavirus disease 2019 and mortality in high-risk patients. Clin Infect Dis. 2023;76(3):e342-e349.