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Commentary

Use of Molnupiravir for COVID-19 Patients in Japan

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Abstract

Molnupiravir (MPV) is a new oral agent for treating SARS-CoV-2 infection, and it was approved for use in COVID-19 patients in Japan in December 2021. A total of 35 COVID-19 patients who received MPV from January 2022 to May 2022 in our hospital were investigated, and their outcomes were compared with those of patients who received intravenous administration of sotrovimab alone and remdesivir (RDV); 32/35 (91.4%) patients who received orally MPV received intravenous administration of sotrovimab in combination, and they were significantly younger than the 14 COVID-19 patients who received sotrovimab alone. Patients with moderate disease were included among those treated with MPV, but all 35 of the patients survived, although one of the patients with mild COVID-19 who received sotrovimab alone died. Furthermore, the patients who received MPV were older, but they could start treatment earlier than the patients who received intravenous administration of RDV. These data suggest that MPV was efficacious for adult COVID-19 patients who could tolerate drugs orally at the appropriate time and became a candidate agent in Japan, as well as intravenous administration therapy by sotrovimab and RDV, in the era of omicron strains.

Key words: Antimicrobial stewardship; Molnupiravir; Remdesivir; SARS-CoV-2; Sotrovimab.

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Brief report

The coronavirus disease 2019 (COVID-19) pandemic has been a huge issue in the world, including Japan, but intravenous antiviral agents, including remdesivir (RDV), and sotrovimab, one of the neutralizing agents, were developed for the treatment of COVID-19 and have shown efficacy in clinical settings [1]. These agents are administered intravenously and usually require hospitalization and care by medical staff. Therefore, development of quicker and more easily administrable agents, such as oral anti-viral drugs, has been awaited.

In December 2021, the oral anti-viral agent molnupiravir (MPV) was approved for use in Japan. The efficacy and safety of MPV treatment were confirmed, and it was recommended to start it within 5 days after the onset of COVID-19 for patients with at least one risk factor for severe COVID-19 illness [2].

In our tertiary hospital, physicians specialized in infectious diseases, pulmonary diseases, emerging and critical care, and surgery established a management team collaborated with the pharmacists to perform team medicine for COVID-19 patients. From January 2022 to May 2022, which was the period when the omicron variant was dominant in Japan, MPV was given to 35 patients (male 19, female 16; age 67.3 (26-90) years) (Table 1). Of the 35 patients who received MPV, 32 (91.4%) were treated with sotrovimab in combination. Compared with the patients who received sotrovimab alone and RDV in the same period, the patients who received MPV were significantly younger than the 14 patients who could not tolerate oral intake of MPV and received sotrovimab alone. The numbers of mild: the cases with no pneumonia, and moderate: the case with pneumonia but oxygen was supplied less than 3L/min, were 20 and 15, respectively, in the patients treated with MPV, although all 14 patients who received sotrovimab alone were mild cases. None of the patients treated with MPV died, although one (1/14=7.1%) of the patients with mild COVID-19 who received sotrovimab alone died. The risk factors, including diabetes, malignancies, obesities, and chronic lung/heart/kidney diseases were not significantly different between the groups (data not shown).

	Molnupiravir (+Sotrovimab)	**Sotrovimab**	**Remdesivir (+Sotrovimab)**	**p value**
Patients number	35	14	26	
Male (Female)	19 (16)	9(5)	16(10)	p=0.531
Age	67.3 (26-90)	79.0 (63-92)	59.3 (36-97)	p<0.001
Severity				p<0.01
Mild	30	14	19	
Moderate	15	0	7	
Drug Administration				p<0.001
Alone	3	14	0	
with Sotrovimab	32	0	26	
Survive (Death)	35 (0)	13 (1)	26 (0)	p=0.383

Table 1: Comparisons of molnupiravir-treated cases with sotrovimab- or remdesivir-treated cases.

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In addition, compared with the 26 patients who received intravenous RDV in the same period, the patients who received MPV were significantly older. Of the 26 patients who received RDV, there were 19 mild and 7 moderate cases, and 26 patients received not only RDV, but also sotrovimab. The patients who received RDV were younger (59.3, range 36-97 years, p<0.001, Table 1), but they might have become more severe because their treatment was delayed compared with the patients who received sotrovimab alone and the patients who received MPV (Figure 1, p=0.048). However, all 26 patients who received RDV survived, similar to the patients who received MPV.

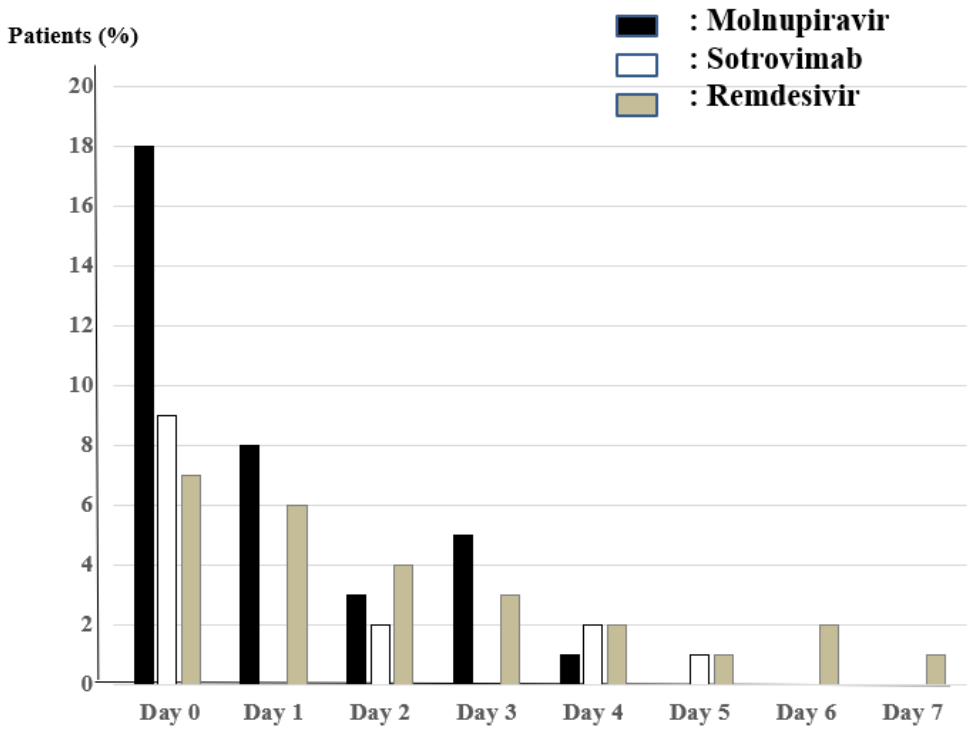

Figure 1: Day from COVID-19 onset for starting molnupiravir, sotrovimab, and remdesivir. Black bars: molnupiravir, white bars: sotrovimab, gray bars: remdesivir, respectively.

Another oral anti-viral agent, nirmatrelvir/ritonavir was also accepted to use in Japan at February 2022 [3], but this agent has a lot of contraindications because of interaction with other common drugs including statins and sleep-inducing drugs, therefore, only two patients were received during the same period (data not shown).

Conclusion

Oral administration of MPV and intravenous administration of sotrovimab were prescribed for mild to moderate COVID-19 patients at high risk, and intravenous administration of RDV was usually recommended for moderate to severe cases according to the guidelines [1, 4]. There are no clinical data on combination treatment, but no significant side effects, such as diarrhea, nausea, vertigo, or liver

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dysfunction, were observed although our data were from small number. Most patients had received two doses of vaccines in all three groups (data not shown). MPV, including MPV and sotrovimab combination therapy, might be useful and became candidate regimens in Japan for mild to moderate COVID-19 patients who can tolerate oral intake early after onset.

Ethics and statistical analysis

The analysis was approved by the Committee for Clinical Scientific Research of Saitama Medical University International Medical Center on July 6, 2022 (#2022-032), and the patients provided written, informed consent for use of their specimens, although the samples were collected as part of routine laboratory analyses.

References

1. Bhimraj A, Morgan RL, Shumaker AH, Lavergne V, Baden L, Cheng VC, et al. Infectious Diseases Society of America Guidelines on the treatment and management of patients with coronavirus disease 2019 (COVID-19). Clin Infect Dis. 2020. PubMed | CrossRef
2. 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. NEJM. 2022;386(6):509-20. PubMed | CrossRef
3. Najjar-Debbiny R, Gronich N, Weber G, Khoury J, Amar M, Stein N, et al. Effectiveness of Paxlovid in Reducing Severe COVID-19 and Mortality in High Risk Patients. Clin Infect Dis. 2022. PubMed | CrossRef
4. Siemieniuk R, Rochwerg B, Agoritsas T, Lamontagne F, Leo YS, Macdonald H, et al. A living WHO guideline on drugs for covid-19. BMJ. 2020;370:m3379. PubMed | CrossRef

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