Infect Chemother. 2022 Mar;54(1):91-101
https://doi.org/10.3947/ic.2021.0140
pISSN 2093-2340·eISSN 2092-6448

Infection & Chemotherapy

Original Article

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Effectiveness of Regdanvimab at Preventing the Need for Oxygen Therapy in Patients with Mild-to-Moderate COVID-19: A Retrospective Cohort Study

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OPEN ACCESS

Received: Dec 14, 2021
Accepted: Feb 27, 2022
Published online: Mar 8, 2022

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ABSTRACT

Background: Monoclonal antibodies are a treatment option for patients with mild-to-moderate coronavirus disease (COVID-19). We investigated the effectiveness of regdanvimab, an anti-severe acute respiratory syndrome coronavirus-2 monoclonal antibody approved in Korea, in the treatment of patients with mild-to-moderate COVID-19.
Materials and Methods: Medical records of patients who were admitted to a COVID-19 designated hospital during the study period of February 1 to June 31 and met the indications for administration of regdanvimab were reviewed to assess baseline characteristics and clinical outcomes such as supplemental oxygen requirements, mortality, and length of hospitalization. Multivariable logistic regression analysis was conducted to identify factors associated with requiring supplemental oxygen. Subgroup analysis was performed according to the presence of pneumonia confirmed on a chest X-ray.
Results: Three hundred ninety-eight COVID-19 patients were included in the study, and 65 (16.3%) of them were administered regdanvimab. The proportion of patients requiring supplemental oxygen was significantly lower in the regdanvimab group than in the control group (6.2% *vs.* 20.1%, $P = 0.007$). There was no significant difference in mortality (0% *vs.* 1.5%, $P > 0.999$) and the length of hospitalization (median: 10 days *vs.* 10 days, $P = 0.267$) between two groups. The multivariable analysis demonstrated that administration of regdanvimab was independently associated with lower oxygen supplement [odds ratio (OR): 0.20, 95% confidence interval (CI): 0.06 - 0.55, $P = 0.004$] after adjustment of potential risk factors related to supplemental oxygen including age, sex, chest X-ray abnormality, and underlying chronic kidney disease. Among the patients with pneumonia radiologically, administration of regdanvimab was also associated with lower risk of oxygen supplement (OR: 0.13, 95% CI: 0.02 - 0.46, $P = 0.007$).
Conclusion: Regdanvimab use was related to lower need for supplemental oxygen in patients with mild-to-moderate COVID-19 for the indications for administration of regdanvimab.

Keywords: SARS-CoV-2; Monoclonal antibody; Immunotherapy; Inpatient care

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Funding
None.

Conflict of Interest
No conflict of interest.

Authors contributions
Conceptualization: EL. Data curation: SJC, EL. Formal analysis: SJC. Investigation: SJC, EL. Methodology: EL. Project administration: EL. Resources: EL. Software: SJC. Supervision: SWP, EL. Validation: SJC, SWP, EL. Visualization: SJC, EL. Writing - original draft: SJC. Writing – review & editing: SWP, EL.

BACKGROUND

The coronavirus disease 2019 (COVID-19) pandemic that started in December 2019 continues to affect millions of people worldwide [1, 2]. The clinical spectrum of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is diverse. Although most people with SARS-CoV-2 infection experience mild disease with spontaneous resolution, some individuals, particularly those who have risk factors such as older age, obesity, diabetes, cardiovascular disease, and chronic lung disease, develop a critical illness that requires intensive care, including mechanical ventilation [3-6].

Comprehensive efforts have been made to develop therapeutic agents for treating COVID-19. These include neutralizing monoclonal antibodies against SARS-CoV-2. The World Health Organization recommends anti-SARS-CoV-2 monoclonal antibodies for the treatment of individuals with mild-to-moderate COVID-19 [7].

Three anti-SARS-CoV-2 monoclonal antibody products have been granted Emergency Use Authorization by the United States Food and Drug Administration (US FDA) for use in non-hospitalized patients with mild-to-moderate COVID-19 who are at high risk of developing the severe disease: bamlanivimab/etesevimab (Eli Lilly and Co., Indianapolis, IN, USA), sotrovimab (GlaxoSmithKline, London, United Kingdom), and casirivimab/imdevimab (Regeneron Pharmaceuticals, New York, NY, USA). Bamlanivimab/etesevimab has been reported to be associated with a 70% reduction in the risk of COVID-19-related hospitalization or death compared to placebo [8]; however, this product has limited effectiveness against the Beta (B.1.351) and Gamma (P.1) variants of SARS-CoV-2 [9]. Sotrovimab has been reported to reduce the risk of hospitalization and death by 85.0% and has been approved for the treatment of non-hospitalized patients with mild-to-moderate COVID-19 in many countries, including the United States, Canada, Singapore, Australia, and Japan [10]. Casirivimab/imdevimab has been reported to reduce the risk of hospitalization and death by approximately 70.0% [11, 12].

Regdanvimab (Celltrion, Incheon, Korea) is an anti-SARS-CoV-2 monoclonal antibody that has been approved in-Korea, Indonesia, and Brazil for the treatment of mild-to-moderate COVID-19. In an interim analysis of a clinical trial published as a preprint, treatment with regdanvimab was associated with a decreased risk of requiring supplemental oxygen or hospital admission in non-hospitalized COVID-19 patients compared to placebo [13]. Based on this result, the Korean Ministry of Food and Drug Safety granted conditional marketing authorization for the emergency use of regdanvimab for the treatment of mild-to-moderate COVID-19 on February 5, 2021.

In this study, we investigated the effectiveness and safety of regdanvimab in hospitalized patients with mild-to-moderate COVID-19 under conditions of standard clinical use.

MATERIALS AND METHODS

1. Patients and data collection

In this retrospective cohort study, we analyzed data from the medical records of patients with COVID-19 who were admitted to a hospital in Seoul, Korea designated for treating COVID-19 between February 1 and June 31, 2021. The hospital has 765 inpatient beds, including 195 nationally designated negative-pressure isolation units, and can accommodate 180 COVID-19

https://doi.org/10.3947/ic.2021.0140

patients. It admits all high-risk patients with COVID-19, regardless of their age and symptoms, and also admits low-risk patients with COVID-19 if they require hospitalization. Some low-risk patients with COVID-19 are admitted to COVID-19 designated community centers for isolation and are transferred to the hospital when hospitalization is required. Among the patients hospitalized during the study period, patients who were treated with regdanvimab during their hospitalization were selected. Patients who met the criteria for regdanvimab administration but did not receive it were selected as a control group. Regdanvimab (Celltrion, Korea) was approved in Korea in February 2021 for administration to patients with mild-to-moderate COVID-19 who do not require oxygen treatment and who meet at least one of the following criteria: are within 7 days of symptom onset, are aged 60 years or older, have abnormalities on chest X-ray, or have more than one underlying comorbidity, such as cardiovascular disease, chronic respiratory disease, diabetes mellitus, or hypertension. We excluded patients younger than 18 years, pregnant women, asymptomatic patients, and patients who required oxygen therapy on the day after admission. Information was collected for on sex, body mass index (BMI), presence of symptoms, and the presence of lung infiltration on chest X-ray according to the chest radiography report. We also collected information on comorbidities including chronic kidney disease (CKD), cancer, and an immunocompromised state. CKD was defined as a glomerular filtration rate <60 mL/min/1.73 m^2 or being on dialysis. In addition, we also collected the status of COVID-19 vaccination in patients. The clinical outcome measures used in the analysis were a requirement for supplemental oxygen, mortality during hospitalization, and the length of hospitalization. The clinical spectrum of COVID-19 was described according to the COVID-19 Treatment Guidelines by the National Institute of Health [9].

2. Ethics statement

This study was approved by the Institutional Review Board of the Seoul Metropolitan Government Boramae Medical Center (No. 20-2021-53). The IRB waived the requirement for informed consent from the study participants because of the retrospective study design.

3. Statistical analysis

Patients were divided into a regdanvimab group and a control group in the analysis. Patient descriptive characteristics were summarized as counts and percentages or medians and interquartile ranges (IQRs). Baseline characteristics of the regdanvimab group and the control group were compared using chi-square tests or Fisher's exact test for categorical variables, and the Mann-Whitney *U*-test for continuous variables. Logistic regression was used to identify factors associated with requiring supplemental oxygen. Multivariable logistic regression analysis was performed with the variables that were statistically significant in univariate logistic regression analysis. The results of the logistic regression analyses were reported as odds ratios (ORs) with 95% confidence intervals (CIs). *P*-values <0.05 were considered statistically significant. All analyses were performed using R Version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

1,171 patients with COVID-19 were admitted to the study hospital during the study period. We excluded 773 patients who were younger than 18 years, pregnant, asymptomatic, received early oxygen therapy, or did not meet the criteria for regdanvimab administration (**Fig. 1**). A total of 398 patients were eligible for regdanvimab administration. Of the 398 patients, 65 (16.3%) received regdanvimab (**Table 1**). The patients in the regdanvimab group were significantly

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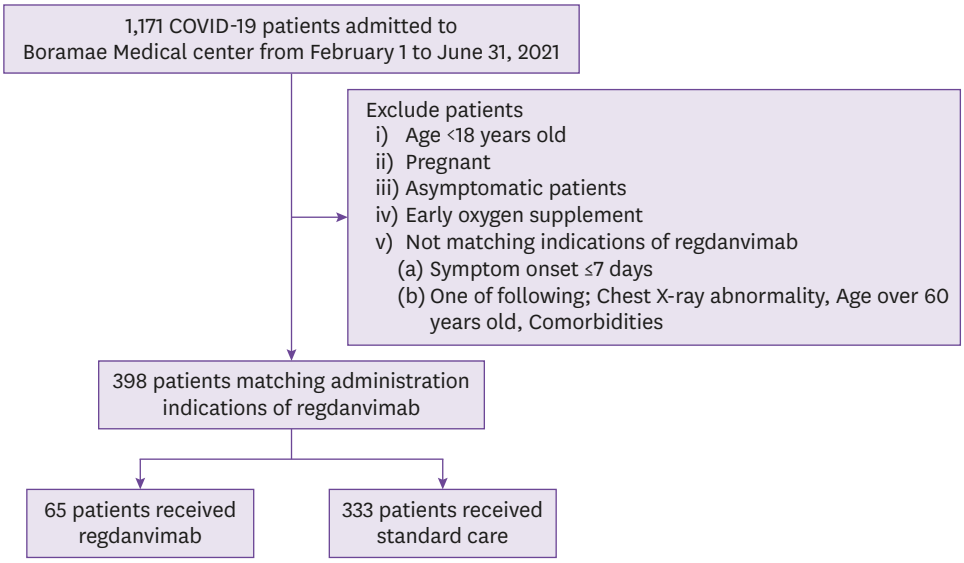

Figure 1. Flow diagram of patient's selection for retrospective cohort study.
COVID-19, coronavirus disease 2019.

Table 1. Baseline Characteristics and clinical outcomes of COVID-19 patients who match the indications of regdanvimab administration

	Regdanvimab (N = 65)	Control (N = 333)	*P*
Age years [median (IQR)]	66 (57 - 75)	60 (48 - 68)	0.001
Male sex [N (%)]	29 (44.6)	149 (44.7)	>0.999
BMI [median (IQR)]	22.78 (20.82 - 26.72)	23.62 (21.45 - 25.96)	0.436
Chest X-ray abnormality [N (%)]	30 (50.8)	211 (63.4)	0.077
Comorbidity [N (%)]			
Hypertension	32 (49.2)	120 (36)	0.062
Cardiovascular disease	7 (10.8)	29 (8.7)	0.769
Diabetes	13 (20)	75 (22.5)	0.776
Chronic pulmonary disease	6 (9.2)	32 (9.6)	>0.999
Chronic kidney disease	2 (3.1)	9 (2.7)	0.697
Cancer	4 (6.2)	14 (4.2)	0.512
Immunosuppression	2 (3.1)	5 (1.5)	0.321
Vaccination[a] [N (%)]	5 (7.7)	17 (5.1)	0.590
Complete vaccination[b] [N (%)]	1 (1.5)	2 (0.6)	0.415
Days from Sx. onsets to admission [median (IQR)]	2 (1 - 3)	3 (2 - 5)	<0.001
Days from diagnosis to admission [median (IQR)]	0 (0 - 1)	0 (0 - 2)	0.081
Duration of Sx. before infusion [median (IQR)]	4 (3 - 5)		
Days from admission to infusion [median (IQR)]	2 (1 - 3)		
Oxygen requirement [N (%)]	4 (6.2)	67 (20.1)	0.007
Oxygen supplement via NP	3 (4.6)	50 (15.0)	0.026
Oxygen supplement via HFNC	1 (1.5)	14 (4.2)	0.482
Oxygen supplement via MV	0 (0.0)	3 (0.9)	>0.999
Duration of Sx. before oxygen requirement [median (IQR)]	10.5 (8.75 - 11.75)	8 (5 - 9)	0.108
Days from admission to oxygen requirement [median (IQR)]	10 (7.75 - 11)	3 (2 - 5)	0.008
In-hospital mortality [N (%)]	0 (0.0)	5 (1.5)	>0.999
Admission duration (days) [median (IQR)]	10 (9 - 11)	10 (8 - 11)	0.267

[a]History of at least one dose of any COVID-19 vaccination.
[b]Diagnosed with COVID-19 after 2 weeks of final doses of COVID-19 vaccinations.
COVID-19, coronavirus disease 2019; N, number; IQR, interquartile range; BMI, body mass index; Sx., symptoms; NP, nasal prong; HFNC, high flow nasal cannula; MV, mechanical ventilator.

older than those in the control group (median age: 66 years *vs.* 60 years, $P = 0.001$). The majority of patients in both groups were female. The median BMI did not differ significantly according to group (median 22.78 *vs.* 23.62 kg/m^2, $P = 0.436$). Chest X-ray abnormalities were

https://doi.org/10.3947/ic.2021.0140

less common among patients in the regdanvimab group than those in the control group (50.8 *vs.* 63.4%, $P = 0.077$). There was no significant difference between groups in the prevalence of underlying comorbidities or the use of immunosuppressive drugs. 22 patients (5.5%) had a history of at least one dose of any COVID-19 vaccination and there was no significant difference between groups in the status of vaccination. Patients in the regdanvimab group and the control group were usually admitted on the day of diagnosis and the median duration from symptom onset to hospitalization was 2 and 3 days, respectively ($P < 0.001$). Patients in the regdanvimab group were administered regdanvimab a median of 4 days after symptom onset (IQR: 3 - 5 days) and 2 days after admission (IQR: 1 - 3 days). The frequency of supplemental oxygen use was significantly lower in the regdanvimab group than in the control group (6.2% *vs.* 20.1%, $P = 0.007$). Most patients who received oxygen therapy (53/71, 74.6%) were provided with low-flow oxygen. The time from symptom onset to starting supplemental oxygen was longer in the patients in the regdanvimab group than those in the control group (median 10.5 days *vs.* 8 days), but the difference was not statistically significant ($P = 0.108$) The time from admission to starting supplemental oxygen was significantly longer in the patients in the regdanvimab group (median 10 days *vs.* 3 days, $P = 0.008$). There were no deaths in the regdanvimab group and five deaths in the control group (0% *vs.* 1.5%, $P > 0.999$). All patients with fatal outcomes were aged >70 years and had multiple underlying comorbidities (**Supplementary Table 1**). Although all patients with fatal outcomes were treated with remdesivir and steroids, they all developed progressive COVID-19 pneumonia. Methicillin-susceptible *Staphylococcus aureus* was isolated from the sputum specimen of one patient with a fatal outcome; however, he received adequate antibiotics and combined bacterial pneumonia did not appear to be the cause of death. The median length of hospitalization was 10 days in both the regdanvimab group and the control group ($P = 0.267$).

In the univariable logistic regression analysis, increasing age, male sex, abnormal findings on chest X-ray, and underlying CKD were found to be associated with an increased risk of requiring supplemental oxygen, and administration of regdanvimab was associated with a decreased risk of requiring supplemental oxygen (**Table 2**). In the multivariable logistic regression analysis, older age (OR: 1.04, 95% CI: 1.02 - 1.06, $P < 0.001$), chest X-ray abnormalities (OR: 3.57, 95% CI: 1.88 - 7.23, $P < 0.001$) were associated with a significantly higher risk of requiring supplemental oxygen. After adjustment of age, sex, chest X-ray abnormalities, and underlying CKD,

Table 2. Univariate and multivariable logistic regression analyses for supplemental oxygen

	Univariable			Multivariable		
	OR	95% CI	*P*	OR	95% CI	*P*
Age	1.02	1.01 - 1.04	0.007	1.04	1.02 - 1.06	<0.001
Sex (male)	1.77	1.06 - 2.98	0.031	1.73	0.99 - 3.02	0.053
BMI	1.03	0.97 - 1.10	0.365			
Chest X-ray abnormality	3.38	1.84 - 6.67	<0.001	3.57	1.88 - 7.23	<0.001
Comorbidity [N (%)]						
Hypertension	1.32	0.78 - 2.22	0.296			
Cardiovascular disease	1.12	0.44 - 2.55	0.792			
Diabetes	1.49	0.82 - 2.64	0.177			
Chronic pulmonary disease	0.85	0.31 - 1.99	0.729			
Chronic kidney disease	5.94	1.74 - 21.18	0.004	3.36	0.88 - 13.66	0.077
Cancer	0.56	0.09 - 2.04	0.451			
Immunosuppression	1.87	0.26 - 8.86	0.461			
Days from Sx. onsets to admission	1.00	0.90 - 1.11	0.994			
Days from diagnosis to admission	1.05	0.92 - 1.19	0.456			
Regdanvimab administration	0.26	0.08 - 0.66	0.012	0.20	0.06 - 0.55	0.004

OR, odds ratio; CI, confidence interval; BMI, body mass index; Sx., symptoms.

https://doi.org/10.3947/ic.2021.0140

administration of regdanvimab remained associated with a significantly lower risk of requiring supplemental oxygen (OR: 0.20, 95% CI: 0.06 - 0.55, $P = 0.004$).

As chest X-ray abnormalities were strongly associated with requiring supplemental oxygen and were more frequent in the control group, we performed subgroup analysis according to the presence of chest X-ray abnormalities to determine whether the more frequent requirement of oxygen treatment in the control group could be attributed to the higher frequency of chest X-ray abnormalities. In patients without chest X-ray abnormalities, there was no difference between groups in age or oxygen requirement (**Supplementary Table 2**). The time from admission to starting oxygen was longer in patients of the regdanvimab group than those in the control group (median: 11 *vs.* 7 days, $P = 0.037$). In patients with chest X-ray abnormalities, those in the regdanvimab group were older than those in the control group (median age: 71 years *vs.* 57 years, $P < 0.001$). The frequency of supplemental oxygen use was significantly lower in the regdanvimab group than in the control group (6.1% *vs.* 26.5%, $P = 0.008$). Univariable logistic regression analysis revealed that increasing age was associated with a higher risk of requiring supplemental oxygen therapy in the patients without chest X-ray abnormalities (**Supplementary Table 3**). In the patients with chest X-ray abnormalities, increasing age was associated with a higher risk of requiring supplemental oxygen, and administration of regdanvimab was associated with a lower risk of requiring supplemental oxygen in the univariable logistic regression analysis. In the multivariable logistic regression analyses with variables including age, sex, CKD, and regdanvimab administration, older age (OR: 1.03, 95% CI: 1.01 - 1.05, $P = 0.003$) was associated with a significantly higher risk of requiring supplemental oxygen, and administration of regdanvimab was associated with a significantly lower risk of requiring supplemental oxygen (OR: 0.13, 95% CI: 0.02 - 0.46, $P = 0.007$).

None of the patients who received regdanvimab experienced hypersensitivity reactions or infusion reactions. One patient reported urticaria on both arms one day after receiving a regdanvimab infusion. There were no serious adverse reactions recorded in the electronic medical records.

DISCUSSION

This study investigated the effectiveness of regdanvimab for the treatment of mild-to-moderate COVID-19. Patients in the regdanvimab group were significantly less likely to require supplemental oxygen than patients in the control group, and regdanvimab administration was independently associated with a reduced likelihood of requiring supplemental oxygen during hospitalization after controlling for confounders. However, there was no statistically significant difference in the mortality rate or the length of hospitalization between the two groups. Statistical analysis of the mortality was limited because of the limited number of patients and the low mortality rates among patients in the study. However, the cause all patients died because of the progression of COVID-19, and there were no deaths due to worsening of underlying diseases not related to COVID-19 or to secondary bacterial infection. A further nationwide study is needed to determine the effectiveness of regdanvimab for preventing death in COVID-19 patients, considering the low mortality rate among COVID-19 patients who do not require supplemental oxygen on admission (0.034%, 65/1,914) [14], and the lack of fatal cases among the 307 patients who participated in the clinical trial of regdanvimab [13].

https://doi.org/10.3947/ic.2021.0140

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Older age, male sex, chest X-ray abnormalities, and CKD have previously been identified as risk factors for severe COVID-19 [4-6, 15, 16], and were significantly associated with requiring supplemental oxygen in this study. However, obesity, which is also known to be a risk factor for severe disease [17], was not significantly associated with requiring supplemental oxygen in this study. Administration of regdanvimab was significantly associated with a reduced likelihood of requiring supplemental oxygen, even after adjusting for age, sex, the presence of chest X-ray abnormalities, and CKD. Subgroup analysis according to the presence of chest X-ray abnormalities revealed that among patients in the regdanvimab group, the frequency requiring supplemental oxygen was similar in those with chest X-ray abnormalities and those without chest X-ray abnormalities. However, among patients in the control group, the frequency of requiring supplemental oxygen was higher in those with chest X-ray abnormalities than those without chest X-ray abnormalities. Administration of regdanvimab was associated with a decreased likelihood of requiring supplemental oxygen in patients with chest X-ray abnormalities. This finding suggests chest X-ray abnormality is an important indicator of which patients are most likely to benefit from regdanvimab administration.

Vaccination is an important factor related to the severity of COVID-19. However, a small number of patients in this study were vaccinated because the study period was before or at the beginning of the COVID-19 vaccination. In addition, there were only three patients who were diagnosed with COVID-19 more than two weeks after the end of vaccination. Further study is needed to investigate the effectiveness of regdanvimab for patients with COVID-19 after vaccination.

In Korea, patients without risk factors for disease progression are primarily admitted to community treatment centers, which are facilities that provide minimum tests and few medications [18]. Patients with worsening symptoms or risk factors for disease progression are admitted or transferred to hospitals. The disease severity of patients in this study is likely to have been more severe than that of patients who participated in clinical trials because we only included hospitalized patients, although most patients who meet the indications for regdanvimab administration are hospitalized. This may explain the higher proportion of patients that required supplemental oxygen in this study than in the clinical trials [13]. Recently, another retrospective cohort study about the effectiveness of the regdanvimab under conditions of standard clinical use was published [19]. It found that administration of regdanvimab was associated with a reduced risk of hypoxemia requiring supplemental oxygen in the total cohort. Although, in the propensity-matched cohort analysis, the reduction in the likelihood of requiring supplemental oxygen among the patients who received regdanvimab was not statically significant, patients in the regdanvimab group were less likely to require supplemental oxygen than the propensity-matched controls. This is similar to our findings and suggests that the administration of regdanvimab to high risk COVID-19 patients can prevent disease progression and the requirement for supplemental oxygen under conditions of standard clinical use.

The length of hospitalization was similar between patients in the regdanvimab group and the control group. This may not adequately represent the effects of regdanvimab because a minimum of 10 days of hospitalization after symptom onset is a governmental requirement in Korea. This could have masked any effect of regdanvimab on reducing the length of hospitalization in patients with COVID-19 under conditions of standard clinical use.

In this study, more than half of the patients met the indication for regdanvimab, but, did not administrate the drug. Although it is difficult to know the reason for not using regdanvimab

https://doi.org/10.3947/ic.2021.0140

frequently in real clinics, we inferred several reasons. First, regdanvimab was available under emergency use authorization with insufficient in-vitro and clinical evidence. In addition, there was insufficient clinical experience from other countries because regdanvimab was first released only in Korea. Second, the indication of regdanvimab is for mild-to-moderate COVID-19 infection which does not need oxygen supplement, therefore, clinicians could consider the risk-benefit of regdanvimab rather than direct clinical usage of the drug in that situation. This can be inferred from that a large number of patients who received regdanvimab were the patients admitted to the department of infectious disease: 49 patients in 159 patients admitted to the department of infectious disease administered regdanvimab (30.8%) and 16 patients in 239 patients admitted to the department of other internal medicine administered regdanvimab (6.7%). Also, the indication of regdanvimab is abnormal chest X-ray, however, other clinical importance such as patients' symptoms rather than just chest X-ray could be the indicator of decisions in real clinics. Lastly, not widely informed the regdanvimab to healthcare providers, they could reluctant to the administration of regdanvimab.

This study has some limitations. It was a retrospective cohort study. It was difficult to find an appropriate control group because of the heterogeneity of the disease manifestations. To overcome this limitation, we restricted the control group to patients who had indications for regdanvimab administration. Nevertheless, patients in the regdanvimab group were significantly older than patients in the control group and abnormalities on the initial chest X-ray were more common in patients who did not receive regdanvimab. To overcome this, we performed multivariable analysis and subgroup analysis. These analyses confirmed that the administration of regdanvimab was associated with a reduced likelihood of requiring supplemental oxygen. Another limitation of the retrospective cohort study was the incomplete medical records. Although we reviewed adverse reactions related to regdanvimab, it is possible that adverse reactions were under-ascertained because they may not have been reported in patients' medical records.

In addition, SARS-CoV-2 variants were not investigated in this study. Mutations of the SARS-CoV-2 spike protein could affect the effectiveness of anti-SARS-CoV-2 monoclonal antibodies. Bamlanivimab/etesevimab has not been approved because of its limited effectiveness against the SARS-CoV-2 Beta (B.1.351) and Gamma (P.1) variants. In Korea [20], the proportion of COVID-19 cases caused by variant strains was less than 20% during the study period (from February 1 to June 31, 2021), and during the period from April to June 2021, approximately 10% of patients were infected with the Alpha variant. Although we did not perform sequencing of the viruses of patients in our study, it is presumed that most of the patients in our study did not have SARS-CoV-2 variants of concern. Subsequently, novel SARS-CoV-2 variants such as the Delta (B.1.167.2) [21], and Omicron (B.1.1.529) [22] variants have emerged and spread worldwide. The Delta variant has mutations in the RBD of the spike protein that impair the binding affinity of neutralizing monoclonal antibodies targeting the RBD. Of the monoclonal antibodies approved by the US FDA, bamlanivimab does not bind to the Delta variant [23]. In addition, the Omicron variant has more mutations in the spike protein than the Delta variant and escapes neutralizing antibodies elicited by COVID-19 vaccination and natural infection [22, 24, 25]. Regdanvimab is a class I neutralizing monoclonal antibody that blocks ACE2 receptors and binds to the RBD [26, 27]. Although regdanvimab has been shown to reduce the death rate and ameliorate weight loss in ACE2-transgenic mice infected with the Delta variant, it showed reduced binding affinity and susceptibility to regdanvimab, and the neutralizing activity of regdanvimab against the Delta variant was lower than that against the original strain of SARS-VoV-2 *in vitro* [28]. In addition, regdanvimab has reduced neutralizing activity against the

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Omicron variant *in vitro* [29]. The effectiveness of regdanvimab against the Delta and Omicron variants *in vivo* is uncertain and further study is needed.

In conclusion, this study investigated the effectiveness of regdanvimab for the treatment of mild-to-moderate COVID-19 patients under conditions of standard clinical use. In our study, the administration of regdanvimab was related to the lower requirement for supplemental oxygen in eligible patients.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Characteristics of 5 patients with fatal outcomes in the control group

Click here to view

Supplementary Table 2

Baseline characteristics and clinical outcomes of COVID-19 patients who match the indications of regdanvimab administration by Chest X-ray abnormalities

Click here to view

Supplementary Table 3

Univariate and multivariable logistic regression analyses for supplemental oxygen by chest X-ray abnormalities

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