Article

The Effectiveness of the Use of Regdanvimab (CT-P59) in Addition to Remdesivir in Patients with Severe COVID-19: A Single Center Retrospective Study

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Abstract: Introduction: Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus infection [1]. Following the first epidemic that occurred in Wuhan, China in December 2019, there have been 180,654,652 globally confirmed cases until June 2021, of which 3,920,463 have resulted in fatality (case-fatality rate: 2.17%) [2]. In Korea, the first case occurred in January 2020, and by June 2021, 155,572 people were infected, with there being 2015 deaths (case-fatality rate: 1.29%) [2].

1. Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus infection [1]. Following the first epidemic that occurred in Wuhan, China in December 2019, there have been 180,654,652 globally confirmed cases until June 2021, of which 3,920,463 have resulted in fatality (case-fatality rate: 2.17%) [2]. In Korea, the first case occurred in January 2020, and by June 2021, 155,572 people were infected, with there being 2015 deaths (case-fatality rate: 1.29%) [2].
Regarding the clinical course of COVID-19 (based on data before remdesivir and systemic corticosteroids were administered) [3], 80% of patients are asymptomatic or have a mild clinical course, 20% develop severe COVID-19 requiring oxygen therapy, and 5% of patients (a quarter of severe COVID-19 cases) progress to critical COVID-19, which requires tracheal intubation or high-flow oxygen therapy, eventually leading to death in 2.3% of all COVID-19 patients [3].

Through large-scale prospective studies conducted in early 2020, it was recognized that the use of remdesivir and systemic corticosteroids was somewhat effective in reducing this mortality rate [4,5]. Accordingly, since September 2020, remdesivir and systemic corticosteroids have been actively used to treat patients with severe COVID-19 in Korea. Korea’s COVID-19 case fatality rate was 1.58% from January 2020 to August 2020 (deaths/cases = 334/21,177) and 1.25% from September 2020 to June 2021 (deaths/cases = 1681/134,395) [2]. As such, it seems that there is a slight reduction in mortality after the use of both drugs. A recent meta-analysis also revealed a decrease in mortality in patients with severe COVID-19 requiring oxygen therapy, after the use of both drugs; however, the degree of mortality reduction was not sufficient [6].

According to the recent Korea Disease Control and Prevention Agency (KDCA) data, which reviewed 8949 COVID-19 patients in Korea, severe COVID-19 with oxygen treatment requirement was observed in 9.1% (816/8949) of cases, of which 29.2% (238/816) resulted in death [7]. Depending on the study, the mortality rate of severe COVID-19 has been reported to be as low as 10% and as high as 36% [3–5,7–9]. Deaths occur mainly in the elderly (over 60 years of age) and patients with underlying diseases (diabetes mellitus, hypertension, obesity, and chronic heart/kidney/lung disease). In this high-risk group, new drugs other than remdesivir and systemic corticosteroids are urgently needed.

Recently, a monoclonal antibody (mAb) called regdanvimab (CT-P59) was developed by a domestic pharmaceutical company (Celltrion Inc., Incheon, Korea) [10]. Safety and potential antiviral efficacy were confirmed in the phase 1 study [11], and a notable clinical effectiveness was confirmed in a phase 2/3 clinical trial, for treatment of mild or moderate COVID-19 patients (reducing hospitalization and oxygen therapy requirement by half, from 8.7% to 4.0%) [12]. It also showed an effect on recently emerged variants [13]. In Korea, regdanvimab has been actively used to treat high-risk patients with mild-to-moderate COVID-19 since March 2021.

Currently, regdanvimab has no clinical usage for treating patients with severe COVID-19, but it has the potential to be effective such cases, when used early in the course of infection. In this study, we evaluated the clinical outcomes of severe COVID-19, when regdanvimab is used in addition to remdesivir and systemic corticosteroids (the current standard of care for severe COVID-19).

2. Material and Methods
2.1. Study Patients

We retrospectively recruited all severe COVID-19 patients who were admitted and treated with remdesivir and oxygen supplementation at Ulsan University Hospital (UUH) (Ulsan, Korea) from 1 March to 11 May 2021. The recruitment start time was set to 1 March 2021 because regdanvimab has been supplied since the end of February. Since then, regdanvimab has been administered to patients with non-severe COVID-19. Severe COVID-19 patients received remdesivir, and some remdesivir-treated patients had previously been administered regdanvimab because their condition had been non-severe immediately after hospitalization (but progressed to severe COVID-19 during hospitalization). Inclusion criteria and exclusion criteria of the present study were as follows: inclusion criteria (i) those who were diagnosed with COVID-19 and received inpatient treatment at Ulsan University Hospital (UUH) (Ulsan, Korea) from 1 March to 11 May 2021, and (ii) those classified as severe COVID-19 and received remdesivir during the study period; exclusion criteria (i) those who did not receive oxygen therapy.
The diagnosis of COVID-19 was made using the real-time polymerase chain reaction (RT-PCR) test for SARS-CoV-2 using the swab sample obtained from the oropharynx and nasopharynx. Severe COVID-19 was defined as the presence of pneumonia and hypoxia [room air pulse oximetric saturation (SpO$_2$) ≤ 94%], with laboratory-confirmed SARS-CoV-2 infection. Pneumonia was identified radiologically [via chest X-ray (CXR) or computed tomography] by the presence of an infiltrate. Remdesivir (200 mg IV on the first day, and 100 mg IV from the next day, for a total of 5 days) was administered to patients with symptoms for less than 10 days, among patients with severe COVID-19, according to the KDCA guidelines [14]. Regdanvimab (a single IV dose of 40 mg/kg) was administered to patients with non-severe COVID-19 (room air SpO$_2$ > 94%) with laboratory-confirmed SARS-CoV-2 infection, according to the following KDCA guidelines: within 7 days of symptom onset and over 60 years of age, underlying diseases (cardiovascular disease, chronic lung disease, diabetes mellitus, or hypertension), or radiologically identified pneumonia (via CXR or computed tomography) [15].

2.2. Study Design

Data were obtained via medical record review from the time of remdesivir initiation to 8 weeks after. After gathering baseline demographic and clinical data at the time of initiation of remdesivir, the following indicators related to clinical outcomes were collected: oxygen use (including the on/off date), type of respiratory support: oxygen with nasal prong or simple mask, or advanced respiratory support [mask with reservoir bag, high flow nasal cannula (HFNC), non-invasive ventilation, invasive ventilation, or extracorporeal membrane oxygenation (ECMO)], SpO$_2$/fraction of inspired oxygen (FiO$_2$) ratio [16] at the time of initiation of remdesivir, the highest FiO$_2$ during treatment, the lowest SpO$_2$/FiO$_2$ ratio during treatment, CXR scores [17], and survival and hospital discharge.

When a patient was oxygenated via nasal prong, the FiO$_2$ values were calculated as 0.24 at 1 L/min, 0.28 at 2 L/min, 0.32 at 3 L/min, 0.36 at 4 L/min, and 0.4 at 5 L/min. When the patient wore a simple oxygen mask, the FiO$_2$ value was calculated to be 0.4 for 5–6 L/min. A FiO$_2$ value of 0.8 was calculated if the patient was receiving oxygen > 10 L/min with a mask with a reservoir bag [18]. CXR scoring was performed by two thoracic radiologists (W. J. Kwon and S. Lim), with two CXRs at the time around remdesivir start and hospital discharge using the method described in a recent paper [17]. If not discharged until 28 days after starting remdesivir, a CXR around 28 days after remdesivir start was selected as the second point.

After the above investigation, patients were divided into a remdesivir alone group and a regdanvimab/remdesivir group. The outcomes were then analyzed. The present study was approved by the Institutional Review Board of Ulsan University Hospital (IRB number: UUH 2021-06-028).

2.3. Primary and Secondary Outcomes

The primary outcome was oxygen-free days on day 28, which was defined as the number of days that a patient was alive and free from oxygen, calculated from the time of initiation of remdesivir. The concept of oxygen-free days is an application of ventilator-free days [19] and has been used in many recent studies [20,21].

As the secondary outcomes, we analyzed the oxygen-free days (on days 14 and 56), days of oxygen supplementation in surviving patients (on days 14, 28, and 56), the highest FiO$_2$ and lowest SpO$_2$/FiO$_2$ ratio during treatment, CXR improvement, duration of hospital stay, and mortality (on days 14, 28, and 56).

2.4. Statistical Analysis

Chi-square test and Fisher’s exact test were used to compare the categorical variables. An independent Student’s t-test was used to compare the continuous variables. To identify independent factors associated with oxygen-free days on day 28, multiple linear regression analysis was performed using basic demographic variables [age, sex, and body mass index]
(BMI)], baseline severity index (SpO2/FiO2 ratio at the time of initiation of remdesivir), and regdanvimab use. The oxygen supplementation days in surviving patients were estimated using the Kaplan-Meier method and log-rank test. All statistical analyses were performed using SPSS version 24 (IBM Corporation, Armonk, NY, USA). Statistical significance was set at \( p < 0.05 \).

3. Results
3.1. Enrolled Patients and Baseline Characteristics

From 1 March to 11 May 2021, 390 symptomatic or high-risk COVID-19 patients were admitted to the UUH. Of these, 74 patients received regdanvimab. Of the 390 patients, 127 were diagnosed with severe COVID-19 and received remdesivir, but three of them did not receive oxygen supplementation at the start of remdesivir administration and were excluded from the analysis. Accordingly, 124 severe COVID-19 patients who received remdesivir and oxygen therapy were included in the present study. Of these, 25 received both regdanvimab and remdesivir (regdanvimab/remdesivir group) and 99 received only remdesivir (remdesivir alone group) (Figure 1).

![Flowchart of the present study](image)

**Figure 1.** Flowchart of the present study. 390 symptomatic or high-risk COVID-19 patients were hospitalized to UUH from 1 March 1 to 11 May 2021. Of these, 74 patients received regdanvimab. Among 390 hospitalized patients, those receiving remdesivir were selected (\( n = 127 \)). Remdesivir was administered to severe COVID-19 patients with pneumonia (determined via chest imaging) and room air SpO2 ≤ 94%. Three patients were excluded from the study because they did not receive oxygen therapy at the start of remdesivir administration, and finally, 124 severe COVID-19 patients were selected for the current study. Of these, 99 patients were administered only remdesivir, and 25 patients were treated using regdanvimab before remdesivir administration. Regdanvimab was used when room air SpO2 > 94% and chest imaging showed pneumonia, over the age of 60 years, or those with underlying diseases (cardiovascular disease, chronic lung disease, diabetes mellitus, or hypertension).

Abbreviations: COVID-19, coronavirus disease 2019; UUH, Ulsan University Hospital; SpO2, pulse oximetric saturation.

Table 1 shows the baseline characteristics of the two groups. The mean age was 57.59 years, and 43.5% were male. There was no significant difference in demographic characteristics between the two groups, except for BMI, with that of the regdanvimab/remdesivir group being higher than that of the remdesivir alone group [kg/m^2, mean ± standard deviation (SD): 24.94 ± 3.19 vs. 26.79 ± 3.83, \( p = 0.014 \)]. Hypertension was the most common underlying disease (25.8%), followed by dyslipidemia (16.1%), diabetes mellitus (12.9%), neurological disease (4.8%), chronic kidney disease (4.0%), and chronic liver disease...
There was no statistically significant difference in the distribution of underlying diseases between the two groups. The period from symptom onset to hospitalization was slightly shorter in the regdanvimab/remdesivir group (days, mean ± SD: 3.19 ± 3.14 vs. 1.76 ± 3.21, p = 0.045), but there was no difference in the period from symptom onset to remdesivir administration (days, mean ± SD: 5.21 ± 3.29 vs. 5.00 ± 3.12, p = 0.772). In the regdanvimab/remdesivir group, regdanvimab was administered at 3.68 and 1.92 days, on average, from symptom onset and admission, respectively, and the administration of remdesivir was performed at 1.32 days, on average, after regdanvimab administration. Respiratory support at the start of remdesivir administration showed a tendency to receive less advanced support in the regdanvimab/remdesivir group (10.1% vs. 4.0%, p = 0.460), and the SpO2/FiO2 ratio was significantly higher in the regdanvimab/remdesivir group (290.09 ± 69.76 vs. 326.63 ± 62.39, p = 0.018). There was no difference in the baseline CXR severity, and systemic corticosteroids were used in nearly all patients.

### Table 1. Baseline characteristics at initiation of remdesivir administration.

| Variables                  | Total (n = 124) | Remdesivir Alone (n = 99) | Regdanvimab/ Remdesivir (n = 25) | p-Value |
|----------------------------|-----------------|---------------------------|----------------------------------|---------|
| Age (years)                | 57.59 ± 12.24   | 56.64 ± 12.13             | 61.36 ± 12.20                    | 0.085   |
| Age (years), distribution  |                 |                           |                                  | 0.413   |
| 20–29                      | 2 (1.6)         | 2 (2.0)                   | 0 (0.0)                          |         |
| 30–39                      | 8 (6.5)         | 8 (8.1)                   | 0 (0.0)                          |         |
| 40–49                      | 18 (14.5)       | 14 (14.1)                 | 4 (16.0)                         |         |
| 50–59                      | 36 (29.0)       | 29 (29.3)                 | 7 (28.0)                         |         |
| 60–69                      | 47 (37.9)       | 37 (37.4)                 | 10 (40.0)                        |         |
| 70–79                      | 7 (5.6)         | 6 (6.1)                   | 1 (4.0)                          |         |
| 80–89                      | 6 (4.8)         | 3 (3.0)                   | 3 (12.0)                         |         |
| Sex                        |                 |                           |                                  | 1.000   |
| Male                       | 54 (43.5)       | 43 (43.4)                 | 11 (44.0)                        |         |
| Female                     | 70 (56.5)       | 56 (56.6)                 | 14 (56.0)                        |         |
| Body weight (kg)           | 68.56 ± 12.68   | 67.66 ± 11.78             | 72.12 ± 15.52                    | 0.116   |
| Height (cm)                | 164.17 ± 8.52   | 164.35 ± 8.04             | 163.47 ± 10.34                   | 0.645   |
| BMI (kg/m²)                | 25.31 ± 3.40    | 24.94 ± 3.19              | 26.79 ± 3.83                     | 0.014   |
| Race                       |                 |                           |                                  | 1.000   |
| Asian                      | 123 (99.2)      | 98 (99.0)                 | 25 (100.0)                       |         |
| White                      | 1 (0.8)         | 1 (1.0)                   | 0 (0.0)                          |         |
| Underlying diseases        |                 |                           |                                  |         |
| Hypertension               | 32 (25.8)       | 25 (25.3)                 | 7 (28.0)                         | 0.779   |
| Diabetes                   | 16 (12.9)       | 12 (12.1)                 | 4 (16.0)                         | 0.728   |
| Dyslipidemia               | 20 (16.1)       | 15 (15.2)                 | 5 (20.0)                         | 0.551   |
| Chronic heart disease      | 3 (2.4)         | 2 (2.0)                   | 1 (4.0)                          | 0.494   |
| Chronic lung disease       | 3 (2.4)         | 2 (2.0)                   | 1 (4.0)                          | 0.494   |
| Chronic kidney disease     | 5 (4.0)         | 4 (4.0)                   | 1 (4.0)                          | 1.000   |
| Chronic liver disease      | 5 (4.0)         | 3 (3.0)                   | 2 (8.0)                          | 0.264   |
| Rheumatologic disease      | 2 (1.6)         | 2 (2.0)                   | 0 (0.0)                          | 1.000   |
| Neurologic disease         | 6 (4.8)         | 5 (5.1)                   | 1 (4.0)                          | 1.000   |
| Psychiatric disease        | 2 (1.6)         | 2 (2.0)                   | 0 (0.0)                          | 1.000   |
| Active malignancy          | 3 (2.4)         | 2 (2.0)                   | 1 (4.0)                          | 0.494   |
| Days from symptom onset    |                 |                           |                                  |         |
| To admission               | 2.90 ± 3.19     | 3.19 ± 3.14               | 1.76 ± 3.21                      | 0.045   |
| To remdesivir              | NA              | NA                        | 3.68 ± 3.00                      | NA      |
| Days from admission        |                 |                           |                                  |         |
| To remdesivir              | 5.17 ± 3.25     | 5.21 ± 3.29               | 5.00 ± 3.12                      | 0.772   |
| Days from regdanvimab      |                 |                           |                                  |         |
| To remdesivir              | 2.27 ± 2.84     | 2.02 ± 2.89               | 3.24 ± 2.47                      | 0.055   |
| Respiratory support at the time of initiation of remdesivir |          |                           |                                  |         |
| Oxygen with nasal prong or simple mask | 113 (91.1) | 89 (89.9) | 24 (96.0) |   |
| Advanced respiratory support | 11 (8.9)       | 10 (10.1)                 | 1 (4.0)                          |         |
| Mask with reservoir bag    | 2 (1.6)         | 2 (2.0)                   | 0 (0.0)                          |         |
| HFNC                       | 9 (7.3)         | 8 (8.1)                   | 1 (4.0)                          |         |
| NIV                        | 0 (0.0)         | 0 (0.0)                   | 0 (0.0)                          |         |
| Invasive ventilation       | 0 (0.0)         | 0 (0.0)                   | 0 (0.0)                          |         |
| ECMO                       | 0 (0.0)         | 0 (0.0)                   | 0 (0.0)                          |         |
Table 1. Cont.

| Variables | Total (n = 124) | Remdesivir Alone (n = 99) | Regdanvimab/Remdesivir (n = 25) | p-Value |
|-----------|----------------|--------------------------|-------------------------------|--------|
| FI O₂ at the time of initiation of remdesivir | 0.34 ± 0.13 | 0.35 ± 0.14 | 0.30 ± 0.08 | 0.078 |
| SpO₂/FI O₂ ratio at the time of initiation of remdesivir | 297.46 ± 69.67 | 290.09 ± 69.76 | 326.63 ± 62.39 | 0.018 |
| SpO₂/FI O₂ ratio distribution at the time of initiation of remdesivir | | | | |
| 0–99 | 2 (4.0) | 1 (2.0) | 0 (0.0) | 0.213 |
| 100–199 | 8 (6.5) | 7 (7.1) | 1 (4.0) | |
| 200–299 | 39 (31.5) | 33 (33.3) | 6 (24.0) | |
| 300–399 | 69 (55.6) | 54 (54.5) | 15 (60.0) | |
| 400–499 | 5 (4.0) | 2 (2.0) | 3 (12.0) | |
| CXR score at the time of initiation of remdesivir | 5.16 ± 4.31 | 5.42 ± 4.42 | 4.16 ± 3.75 | 0.194 |
| Systemic corticosteroids use | 122 (98.4) | 97 (98.0) | 25 (100.0) | |
| Dexamethasone | 121 (97.6) | 97 (98.0) | 24 (96.0) | |
| Prednisolone | 1 (0.8) | 0 (0.0) | 1 (4.0) | |

Data are presented as mean ± standard deviation or number (%). BMI: body mass index; CXR: chest X-ray; NA: not applicable; HFNC: high flow nasal cannula; NIV: non-invasive ventilation; ECMO: extracorporeal membrane oxygenation; FI O₂: fraction of inspired oxygen; SpO₂: pulse oximetric saturation.

3.2. Primary Outcome

28 days after the initiation of remdesivir administration, the regdanvimab/remdesivir group showed significantly longer oxygen-free days than the remdesivir alone group (days, mean ± SD: 19.36 ± 7.87 vs. 22.72 ± 3.66, p = 0.003) (Table 2).

Table 2. Clinical outcomes of the remdesivir alone group and the regdanvimab/remdesivir group.

| Variables | Total (n = 124) | Remdesivir Alone (n = 99) | Regdanvimab/Remdesivir (n = 25) | p-Value |
|-----------|----------------|--------------------------|-------------------------------|--------|
| Primary outcome | | | | 0.003 |
| Oxygen-free days on day 28 | 20.04 ± 7.33 | 19.36 ± 7.87 | 22.72 ± 3.66 | |
| Median (IQR) | 22.0 (20.0–24.5) | 22.0 (19.0–24.0) | 23.0 (22.0–25.0) | |
| Secondary outcomes | | | | 0.074 |
| Oxygen-free days on day 14 | 7.48 ± 4.15 | 7.14 ± 4.26 | 8.80 ± 3.43 | |
| Median (IQR) | 8.0 (6.0–10.5) | 8.0 (5.0–10.0) | 9.0 (8.0–11.0) | |
| Oxygen-free days on day 56 | 46.85 ± 11.52 | 45.87 ± 12.59 | 50.72 ± 3.66 | |
| Median (IQR) | 50.0 (48.0–52.5) | 50.0 (47.0–52.0) | 51.0 (50.0–53.0) | |
| Oxygen off and live on day 14 | 104 (83.9) | 80 (80.8) | 24 (96.0) | |
| Oxygen off and live on day 28 | 116 (93.5) | 91 (91.9) | 25 (100.0) | |
| Oxygen off and live on day 56 | 119 (96.0) | 94 (94.9) | 25 (100.0) | |
| The highest FI O₂ during treatment | 0.45 ± 0.24 | 0.48 ± 0.26 | 0.34 ± 0.15 | |
| The lowest SpO₂/FI O₂ ratio during treatment | 248.86 ± 89.43 | 237.05 ± 89.68 | 295.63 ± 72.74 | |
| The lowest SpO₂/FI O₂ ratio distribution during treatment | 248.86 ± 89.43 | 237.05 ± 89.68 | 295.63 ± 72.74 | |
| The highest degree of respiratory support during treatment | 0.087 |
| Oxygen with nasal prong or simple mask | 15 (12.1) | 15 (15.2) | 0 (0.0) | |
| Advanced respiratory support | 17 (13.7) | 14 (14.1) | 3 (12.0) | |
| Mask with Reservoir bag | 41 (33.1) | 34 (34.3) | 7 (28.0) | |
| HFNC | 50 (40.3) | 35 (35.4) | 15 (60.0) | |
| NIV | 1 (0.8) | 1 (1.0) | 0 (0.0) | |
| Invasive ventilation | 0 (0.0) | 0 (0.0) | 0 (0.0) | |
| ECMO | 0 (0.0) | 0 (0.0) | 0 (0.0) | |
Table 2. Cont.

| Variables                       | Total (n = 124) | Remdesivir Alone (n = 99) | Regdanvimab/Remdesivir (n = 25) | p-Value |
|---------------------------------|----------------|--------------------------|---------------------------------|---------|
| Changes in CXR                  |                |                          |                                 |         |
| Days from the first scored CXR  | 10.93 ± 6.69   | 11.45 ± 7.03             | 8.96 ± 4.80                     | 0.098   |
| Difference between the two CXR scores (initial minus post) | 1.36 ± 4.66 | 1.58 ± 4.59 | 0.48 ± 4.95 | 0.294 |
| Duration of hospital stay (days) | 15.40 ± 10.38 | 15.67 ± 11.12 | 14.32 ± 6.78 | 0.563 |
| Mortality *                     |                |                          |                                 |         |
| Death at day 14                  | 1 (0.8)        | 1 (1.0)                  | 0 (0.0)                         | 1.000   |
| Death at day 28                  | 2 (1.6)        | 2 (2.0)                  | 0 (0.0)                         | 1.000   |
| Death at day 56                  | 2 (1.6)        | 2 (2.0)                  | 0 (0.0)                         | 1.000   |
| All-cause mortality              | 2 (1.6)        | 2 (2.0)                  | 0 (0.0)                         | 1.000   |

Data are presented as mean ± standard deviation or number (%). SD: standard deviation; IQR: interquartile range; FiO₂: fraction of inspired oxygen; SpO₂: pulse oximetric saturation; HFNC: high flow nasal cannula; NIV: non-invasive ventilation; ECMO: extracorporeal membrane oxygenation; CXR: chest X-ray. * Two deaths occurred: a 78-year-old male and an 83-year-old female died on days 15 and 12, respectively. Their cause of death was COVID-19.

3.3. Secondary Outcomes

In line with the primary outcome, oxygen-free days on days 14 (days, mean ± SD: 7.14 ± 4.26 vs. 8.80 ± 3.43, p = 0.074) and 56 (days, mean ± SD: 45.87 ± 12.59 vs. 50.72 ± 3.66, p = 0.001) were longer in the regdanvimab/remdesivir group. Survivors for whom oxygen supplementation was stopped also showed a higher tendency in the regdanvimab/remdesivir group on days 14 (80.8% vs. 96.0%, p = 0.074), 28 (91.9% vs. 100.0%, p = 0.357), and 56 (94.9% vs. 100.0%, p = 0.582). The regdanvimab/remdesivir group had a lower FiO₂ and higher SpO₂/FiO₂ ratio during treatment (highest FiO₂ during treatment, mean ± SD: 0.48 ± 0.26 vs. 0.34 ± 0.15, p = 0.001; lowest SpO₂/FiO₂ ratio during treatment, mean ± SD: 237.05 ± 89.68 vs. 295.63 ± 72.74, p = 0.003). Respiratory support during treatment tended to receive less advanced support in the regdanvimab/remdesivir group (29.3% vs. 12.0%, p = 0.077). There were no statistical differences in the degree of CXR change, length of hospitalization, and mortality (Table 2).

According to Kaplan-Meier estimates, the durations of oxygen supplementation in survivors were significantly shorter in the regdanvimab/remdesivir group on days 14 (days, mean ± SD: 6.71 ± 4.18 vs. 5.20 ± 3.43, p = 0.046), 28 (days, mean ± SD: 6.71 ± 4.18 vs. 5.20 ± 3.43, p = 0.046), and 56 (days, mean ± SD: 9.31 ± 11.41 vs. 5.28 ± 3.66, p = 0.024), as compared to the remdesivir alone group (Figure 2).

3.4. Independent Factors Associated with Oxygen-Free Days on Day 28

Independent factors associated with oxygen-free days on day 28, identified through multiple linear regression analysis, included regdanvimab use [B: 3.568; 95% confidence interval (CI): 0.596–6.539, p = 0.019], age (per year, B: −0.254; 95% CI: −0.352–−0.156, p < 0.001), and baseline SpO₂/FiO₂ ratio (B: 0.029; 95% CI: 0.013–0.046, p = 0.001) (Table 3).

3.5. Adverse Events Associated with Regdanvimab Use

Of the 25 regdanvimab users, 14 (56%) had no adverse events. However, some users had the following events: fever in 5 patients (20%), dyspnea in 7 patients (28%), nausea in 1 patient (4%), and delirium in 1 patient (4%). However, these adverse events may be a presentation of COVID-19 itself.
3.3. Secondary Outcomes
In line with the primary outcome, oxygen requirement was lower, the SpO$_2$ fraction of inspired oxygen, SpO$_2$: pulse oximetric saturation; FiO$_2$: fraction of inspired oxygen, SpO$_2$: pulse oximetric saturation.

4. Discussion
In severe COVID-19 patients, the use of regdanvimab, in addition to remdesivir, increased the number of oxygen-free days. The oxygen-free days was also independently associated with use of regdanvimab, as determined via multiple linear regression analysis with adjustment of baseline severity and demographic variables including age. In addition, the FiO$_2$ requirement was lower, the SpO$_2$/FiO$_2$ ratio was higher, and oxygen

### Table 3. Factors associated with oxygen-free days on day 28.

| Variables                   | Simple Linear Regression | Multiple Linear Regression |
|-----------------------------|--------------------------|---------------------------|
|                             | $B$          | SE    | $\beta$  | $t$ | $p$-Value | 95% CI for $B$ | $B$ | SE    | $\beta$  | $t$ | $p$-Value | 95% CI for $B$ |
| Regdanvimab use             | 3.356        | 1.619 | 0.184   | 2.073 | 0.040     | 0.151 - 6.562 | 3.568 | 1.501 | 0.196   | 2.377 | 0.019     | 0.596 - 6.539  |
| Age (per year)              | -0.246       | 0.049 | -0.411  | -4.981 | <0.001    | -0.344 - 0.148 | -0.254 | 0.049 | -0.424  | -5.126 | <0.001    | -0.352 - 0.156 |
| Female sex                  | 2.761        | 1.309 | 0.188   | 2.109 | 0.037     | 0.169 - 5.353 | 1.742 | 1.140 | 0.118   | 1.528 | 0.129     | -0.516 - 4.000 |
| BMI (per kg/m$^2$)          | 0.306        | 0.193 | 0.142   | 1.585 | 0.116     | -0.076 - 0.689 | -0.043 | 0.181 | -0.020  | -0.238 | 0.812     | -0.402 - 0.316 |
| Baseline SpO$_2$/FiO$_2$ ratio | 0.040         | 0.029 | 0.383   | 4.582 | <0.001    | 0.0023 - 0.058 | 0.029 | 0.009 | 0.280   | 3.461 | 0.001     | 0.013 - 0.046  |

CI: Confidence Interval; SE: standard error; BMI: body mass index; SpO$_2$: pulse oximetric saturation; FiO$_2$: fraction of inspired oxygen, SpO$_2$: pulse oximetric saturation.

Figure 2. Kaplan-Meier estimates of the remdesivir alone and regdanvimab/remdesivir groups. (A) Days of oxygen supplementation, in surviving patients on day 14, were shorter in the regdanvimab/remdesivir group (days, mean ± SD: 6.71 ± 4.18 vs. 5.20 ± 3.43, $p = 0.046$). (B) Days of oxygen supplementation, in surviving patients on day 28, were shorter in the regdanvimab/remdesivir group (days, mean ± SD: 8.24 ± 7.43 vs. 5.28 ± 3.66, $p = 0.024$). (C) Days of oxygen supplementation, in surviving patients on day 56, were shorter in the regdanvimab/remdesivir group (days, mean ± SD: 9.31 ± 11.41 vs. 5.28 ± 3.66, $p = 0.024$). Abbreviations: SD, standard deviation.
dependence was shorter, in patients using regdanvimab. These findings suggest that the use of regdanvimab, in addition to remdesivir, has a significantly favorable impact on the clinical outcomes of severe COVID-19. Our small-scale retrospective study needs to be validated via a prospective, large-scale study. However, given the current high mortality rate of severe COVID-19, the simultaneous use of regdanvimab and remdesivir could be considered in severe COVID-19.

Hospital admissions or deaths due to COVID-19 have been decreasing with the use of vaccines, and vaccines are effective against recently emerged variants [22]. However, once a person develops COVID-19 severe enough to be hospitalized, the mortality rate is very high, ranging from 10–36% [3–5,7–9]. Although remdesivir and systemic corticosteroids are somewhat effective against severe COVID-19, the associated decrease in mortality rate is insufficient [6]. Deaths from severe COVID-19 occur primarily in people over the age of 60 years and those with underlying medical conditions, and additional new drugs are needed for treating these individuals [3–5,7–9].

Among several candidate drugs, anti-SARS-CoV-2 mAbs against the receptor-binding domain (RBD) of the spike glycoprotein can be effective in severe COVID-19. This is because they have been proven effective in mild and moderate conditions of the same disease [23,24]. When used early in the course of the disease, such drugs inhibit the progression of mild or moderate COVID-19 to severe COVID-19, which requires hospitalization or oxygen supplementation. As of June 2021, anti-SARS-CoV-2 mAbs that have proven their effectiveness through early phase clinical trials and have secured emergency or conditional use authorization include bamlanivimab (Eli Lilly and Company, Indianapolis, IN, USA), a combination of bamlanivimab and etesevimab (Eli Lilly and Company, Indianapolis, IN, USA), and a combination of casirivimab and imdevimab (Regeneron Pharmaceuticals, Eastview/Tarrytown, NY, USA) in the United States, as well as regdanvimab (Celltrion Inc., Incheon, Korea) in Korea [23,24].

Regdanvimab is a potent neutralizing antibody against various SARS-CoV-2 isolates, which blocks the interaction regions of the RBD [meant for binding angiotensin-converting enzyme 2 (ACE2)] of SARS-CoV-2 spike protein [10]. Regdanvimab was found to be effective at reducing viral load and ameliorating clinical symptoms in animal experiments [10], and safety and virologic efficacy were confirmed through two randomized phase 1 clinical trials in healthy adults and patients with mild SARS-CoV-2 infection [11]. A recent phase 2/3 clinical trial demonstrated that the progression rates to severe COVID-19 were reduced by 54% (from 8.7% to 4.0%) for patients with mild to moderate COVID-19 and 68% (from 23.7% to 7.5%) for moderate COVID-19 patients aged 50 years and over. Furthermore, the clinical recovery time was 3.4 to 6.4 days faster in patients treated with regdanvimab, compared to those treated with placebo [12]. Recently published retrospective studies also demonstrated that regdanvimab treatment prevented progression to severe disease [25,26]. Accordingly, in February 2021, the Korean Ministry of Food and Drug Safety approved the conditional marketing authorization for the emergency use of regdanvimab for adult (>18 years) patients with mild to moderate COVID-19, when the following conditions were met: within 7 days of symptom onset and over 60 years of age, underlying disease (cardiovascular disease, chronic lung disease, diabetes mellitus, or hypertension), or radiologically identified pneumonia (either by CXR or computed tomography) [15].

Regdanvimab has been supplied to our hospital (UHH) since the end of February 2021. Since then, regdanvimab has been administered to indicated patients with non-severe COVID-19. Severe COVID-19 patients received remdesivir according to indications, and some remdesivir-treated patients had been treated with regdanvimab because their condition had been non-severe immediately after hospitalization (but progressed to severe COVID-19 during hospitalization). We extracted severe COVID-19 patients who received remdesivir and oxygen therapy after regdanvimab had been supplied and divided them into a group using only remdesivir and a group using both regdanvimab and remdesivir to investigate clinical outcomes.
In our study, the use of regdanvimab in patients with severe COVID-19 significantly increased the number of oxygen-free days, compared to the remdesivir alone group. The use of regdanvimab and increase in oxygen-free days (on day 28) were also significantly associated, as per multiple linear regression analysis that included important clinical indicators such as age, sex, BMI, and baseline SpO$_2$/FiO$_2$ ratio at the time of initiation of remdesivir administration, which represent the initial severity. Furthermore, the use of regdanvimab was associated with lower FiO$_2$ requirement, higher SpO$_2$/FiO$_2$ ratio during treatment, and a shorter duration of oxygen supplementation. These results suggest that the use of regdanvimab in combination with remdesivir has a significant beneficial effect on the clinical outcomes of severe COVID-19.

Some clinical trials involving targeting of severe COVID-19 by mAbs have already been conducted. In the ACTIV-3 trial ($n = 326$, 1:1 randomization), administration of bamlanivimab, in combination with the standard of care (typically being remdesivir administration), did not demonstrate additional clinical benefits in hospitalized patients with severe COVID-19 [27]. However, in the REGN-COV2 trial ($n = 9785$, 1:1 randomization), a combination of two mAbs (casirivimab and imdevimab), in addition to usual care (not fully disclosed yet), reduced the risk of death by 20%, in patients hospitalized with COVID-19 [28]. The full report of the REGN-COV2 trial has not yet been published, so it is difficult to interpret its results, but the difference between the two conflicting results is presumed to be the timing of mAb injection. In the REGN-COV2 trial, mAbs were administered to early phase patients who were seronegative (before developing an immune response to SARS-COV-2). In the ACTIV-3 trial, which showed negative results, mAb administration took a median of 7 (interquartile range: 5–9) days after symptom onset [27]. In our study, it took an average of 3.68 days for regdanvimab to be administered after symptom onset. For mAbs to be effective in viral infectious diseases, they must be administered in the early stages of infectious diseases, when the viral load is high, but before seroconversion occurs [23]. It is difficult to expect the effect of mAbs in the post-viral phase, wherein a secondary immune response is induced after the initial virally driven phase [23].

There were no serious adverse drug reactions related to the administration of regdanvimab. Fewer than 50% of patients had fever and dyspnea while using regdanvimab, which could be symptoms of COVID-19 itself. None of the users stopped taking the drug due to side effects, and all 25 patients were administered the full dose of regdanvimab without any major events. Also in a previous phase 2/3 trial, there were no reports of serious adverse events associated with the use of regdanvimab [12].

Our study has some important limitations. First, patients with relatively mild COVID-19 might have been included in the regdanvimab/remdesivir group, and patients with relatively severe COVID-19 might have been included in the remdesivir alone group; as the baseline SpO$_2$/FiO$_2$ ratio was higher in the regdanvimab/remdesivir group, this is a reasonable deduction. However, we found a significant correlation between regdanvimab administration and oxygen-free days, as per the multivariate analysis, adjusted for the SpO$_2$/FiO$_2$ ratio. And it is also possible that the use of regdanvimab resulted in a relatively mild degree of severe COVID-19. Second, the number of patients was small. Although the results of this study had statistical significance, it is a retrospective, small sample-sized, single-center study; thus, there might be selection bias. Despite these limitations, our study has a novelty in attempting to elucidate the effectiveness of regdanvimab in severe COVID-19.

5. Conclusions

Administration of regdanvimab, in addition to remdesivir, significantly improved clinical outcomes in severe COVID-19. Although results of the present study require confirmation via a large-scale, prospective, randomized study, active consideration of regdanvimab administration in severe COVID-19 is needed to facilitate the reduction of high mortality rate associated with severe COVID-19 and the mild adverse drug reaction associated with regdanvimab administration.
Author Contributions: Conceptualization, G.C., A.C., W.K. and T.L.; Methodology, A.C., E.P. and T.L.; Formal Analysis, A.C., E.P. and T.L.; Data Curation, A.C. and T.L.; Writing—Original Draft Preparation, T.L.; Writing—Review & Editing, G.C., S.L., S.P., S.L., Y.A., J.K., S.R., Y.J., J.A. and J.J. All authors have read and agreed to the published version of the manuscript.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Institutional Review Board Statement: The present study was approved by the Institutional Review Board of Ulsan University Hospital (IRB number: UUH 2021-06-028).

Informed Consent Statement: Patient consent was waived due to the retrospective nature of the study.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Park, S.E. Epidemiology, virology, and clinical features of severe acute respiratory syndrome -coronavirus-2 (SARS-CoV-2; Coronavirus Disease-19). Clin. Exp. Pediatr. 2020, 63, 119–124. [CrossRef] [PubMed]
2. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. Available online: https://covid19.who.int (accessed on 30 June 2021).
3. Wu, Z.; McGoogan, J.M. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020, 323, 1239–1242. [CrossRef]
4. RECOVERY Collaborative Group; Horby, P.; Lim, W.S.; Emberson, J.R.; Mafham, M.; Bell, J.L.; Linsell, L.; Staplin, N.; Brightling, C.; Ustianowska, A.; et al. Dexamethasone in hospitalized patients with COVID-19. N. Engl. J. Med. 2021, 384, 693–704. [CrossRef] [PubMed]
5. Beigel, J.H.; Tomashek, K.M.; Dodd, L.E.; Mehta, A.K.; Zingman, B.S.; Kalil, A.C.; Hohmann, E.; Chu, H.Y.; Luetkemeyer, A.; Kline, S.; et al. Remdesivir for the treatment of COVID-19—final report. N. Engl. J. Med. 2020, 383, 1813–1826. [CrossRef] [PubMed]
6. Lee, T.C.; McDonald, E.G.; Butler-Laporte, G.; Harrison, L.B.; Cheng, M.P.; Brophy, J.M. Remdesivir and systemic corticosteroids for the treatment of COVID-19: A Bayesian re-analysis. Int. J. Infect. Dis. 2021, 104, 671–676. [CrossRef]
7. Lee, J.; Lim, D.S.; Hong, S.O.; Park, M.J.; Kim, G.; Lim, N.-K.; Lee, S.Y.; Park, J.K.; Song, D.S.; Chai, H.Y.; et al. The primary report of clinical data analysis on the COVID-19 in the Republic of Korea. Public Health Wkly. Rep. 2020, 13, 2054–2058.
8. Olivas-Martínez, A.; Cárdenas-Fragoso, J.L.; Jiménez, J.V.; Lozano-Cruz, O.A.; Ortiz-Brizuela, E.; Tovar-Méndez, V.H.; Medrano-Borromeo, C.; Martínez-Valenzuela, A.; Román-Montes, C.M.; Martínez-Guerra, B.; et al. In-hospital mortality from severe COVID-19 in a tertiary care center in Mexico City; causes of death, risk factors and the impact of hospital saturation. PLoS ONE 2021, 16, e0245772. [CrossRef]
9. Wang, Z.; Wang, Z. Identification of risk factors for in-hospital death of COVID-19 pneumonia – lessons from the early outbreak. BMC Infect. Dis. 2021, 21, 113. [CrossRef]
10. Kim, C.; Ryu, D.K.; Lee, J.; Kim, Y.J.; Seo, J.M.; Kim, Y.G.; Jeong, J.H.; Kim, M.; Kim, J.I.; Kim, P.; et al. A therapeutic neutralizing antibody targeting receptor binding domain of SARS-CoV-2 spike protein. Nat. Commun. 2021, 12, 288. [CrossRef]
11. Kim, J.Y.; Jang, Y.R.; Hong, J.H.; Jung, J.G.; Park, J.H.; Streinu-Cercel, A.; Streinu-Cercel, A.; Sândulescu, O.; Lee, S.J.; Kim, S.H.; et al. Safety, Virologic Efficacy, and Pharmacokinetics of CT-P59, a Neutralizing Monoclonal Antibody Against SARS-CoV-2 Spike Receptor-Binding Protein: Two Randomized, Placebo-Controlled, Phase I Studies in Healthy Individuals and Patients With Mild SARS-CoV-2 Infection. Clin. Ther. 2021, 43, 1706–1727. [CrossRef]
12. Eom, J.S.; Ison, M.; Streinu-Cercel, A.; Sândulescu, O.; Preotescu, L.-L.; Kim, Y.-S.; Kim, J.Y.; Cheon, S.H.; Jang, Y.R.; Lee, S.J.; et al. Efficacy and safety of CT-P59 plus standard of care: A phase 2/3 randomized, double-blind, placebo-controlled trial in outpatients with mild-to-moderate SARS-CoV-2 infection. Res. Sq. 2021; in preprint. [CrossRef]
13. Ryu, D.K.; Kang, B.; Noh, H.; Woo, S.J.; Lee, M.H.; Nuijtten, P.M.; Kim, J.I.; Seo, J.M.; Kim, C.; Kim, M.; et al. The in vitro and in vivo efficacy of CT-P59 against Gamma, Delta and its associated variants of SARS-CoV-2. Biochem. Biophys. Res. Commun. 2021, 578, 91–96. [CrossRef]
14. Ministry of Health and Welfare; Korea Disease Control and Prevention Agency (KDCA). Supplying Remdesivir for the Treatment of COVID-19 (Korean). Available online: http://www.mohw.go.kr/react/al/sal0301vwjsp?PAR_MENU_ID=04&MENU_ID=0403&page=1&CONT_SEQ=355233 (accessed on 9 July 2021).
15. Ministry of Health and Welfare; Korea Disease Control and Prevention Agency (KDCA). Guide to Administration Management Plan for COVID-19 Antibody Treatment (Regkirona) (Ver.02) (Release Date: FEB 14, 2021) (Korean). Available online: http://ncov.mohw.go.kr/upload/ncov/file/202108/1627978032143_20210803170712.pdf (accessed on 14 February 2021).
16. Rice, T.W.; Wheeler, A.P.; Bernard, G.R.; Hayden, D.L.; Schoenfeld, D.A.; Ware, L.B.; National Institutes of Health, National Heart, Lung, and Blood Institute ARDS Network. Comparison of the SpO$_2$/FiO$_2$ ratio and the PaO$_2$/FiO$_2$ ratio in patients with acute lung injury or ARDS. Chest 2007, 132, 410–417. [CrossRef]

17. Borghesi, A.; Maroldi, R. COVID-19 outbreak in Italy: Experimental chest X-ray scoring system for quantifying and monitoring disease progression. Radiol. Med. 2020, 125, 509–513. [CrossRef]

18. Choi, K.J.; Hong, H.L.; Kim, E.J. The association between mortality and the oxygen saturation and fraction of inhaled oxygen in patients requiring oxygen therapy due to COVID-19-associated pneumonia. Tuberc. Respir. Dis. 2021, 84, 125–133. [CrossRef]

19. Simonis, F.D.; Serpa Neto, A.; Binnekade, J.M.; Braber, A.; Bruin, K.C.M.; Determann, R.M.; Goekoop, G.J.; Heidt, J.; Horn, J.; Innemee, G.; et al. Effect of a low vs intermediate tidal volume strategy on ventilator-free days in intensive care unit patients without ARDS: A randomized clinical trial. JAMA 2018, 320, 1872–1880. [CrossRef]

20. Waghmare, A.; Xie, H.; Kimball, L.; Yi, J.; Özök, S.; Leisenring, W.; Cheng, G.S.; Englund, J.A.; Watkins, T.R.; Chien, J.W.; et al. Supplemental oxygen-free days in hematopoietic cell transplant recipients with respiratory syncytial virus. J. Infect. Dis. 2017, 216, 1235–1244. [CrossRef]

21. Ulrich, R.J.; Troxel, A.B.; Carmody, E.; Eapen, J.; Bäcker, M.; DeHovitz, J.A.; Prasad, P.; Li, Y.; Delgado, C.; Jrada, M.; et al. Treating COVID-19 with hydroxychloroquine (TEACH): A multicenter, double-blind randomized controlled trial in hospitalized patients. Open Forum Infect. Dis. 2020, 7, ofaa446. [CrossRef]

22. Sheikh, A.; McMenamin, J.; Taylor, B.; Robertson, C.; Public Health Scotland and the EAVE II Collaborators. SARS-CoV-2 Delta VOC in Scotland: Demographics, risk of hospital admission, and vaccine effectiveness. Lancet 2021, 397, 2461–2462. [CrossRef]

23. Taylor, P.C.; Adams, A.C.; Hufford, M.M.; de la Torre, I.; Winthrop, K.; Gottlieb, R.L. Neutralizing monoclonal antibodies for treatment of COVID-19. Nat. Rev. Immunol. 2021, 21, 382–393. [CrossRef]

24. Kim, S.B.; Kim, J.; Huh, K.; Choi, W.S.; Kim, Y.J.; Joo, E.J.; Kim, Y.J.; Yoon, Y.K.; Heo, J.Y.; Seo, Y.B.; et al. Korean Society of Infectious Diseases/National Evidence-based Healthcare Collaborating Agency recommendations for anti-SARS-CoV-2 monoclonal antibody treatment of patients with COVID-19. Infect. Chemother. 2021, 53, 395–403. [CrossRef] [PubMed]

25. Lee, S.; Lee, S.O.; Lee, J.E.; Kim, K.H.; Lee, S.H.; Hwang, S.; Kim, S.W.; Chang, H.H.; Kim, Y.; Bae, S.; et al. Regdanvimab in patients with mild-to-moderate SARS-CoV-2 infection: A propensity score-matched retrospective cohort study. Int. Immunopharmacol. 2022, 106, 108570. [CrossRef] [PubMed]

26. Lee, J.Y.; Lee, J.Y.; Ko, J.H.; Hyun, M.; Kim, H.A.; Cho, S.; Lee, Y.D.; Song, J.; Shin, S.; Peck, K.R. Effectiveness of Regdanvimab Treatment in High-Risk COVID-19 Patients to Prevent Progression to Severe Disease. Front. Immunol. 2021, 12, 772320. [CrossRef] [PubMed]

27. ACTIV-3/TICO LY-CoV555 Study Group; Lundgren, J.D.; Grund, B.; Barkauskas, C.E.; Holland, T.L.; Gottlieb, R.L.; Sandkovsky, U.; Brown, S.M.; Knowlton, K.U.; Self, W.H.; et al. A neutralizing monoclonal antibody for hospitalized patients with COVID-19. N. Engl. J. Med. 2021, 384, 905–914. [CrossRef]

28. Regeneron. REGEN-COV™ (Casirivimab and Imdevimab) Phase 3 Recovery Trial Meets Primary Outcome, Improving Survival in Hospitalized COVID-19 Patients Lacking an Immune Response to SARS-COV-2. Available online: https://investor.regeneron.com/news-releases/news-release-details/regen-covtm-casirivimab-and-imdevimab-phase-3-recovery-trial (accessed on 21 January 2022).