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Effectiveness of regdanvimab on mortality in COVID-19 infected patients on hemodialysis

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Background: Although several therapeutic agents have been evaluated for the treatment of coronavirus disease 2019 (COVID-19), there are lack of effective and proven treatments for end-stage renal disease (ESRD). The present study aims to evaluate the effectiveness of regdanvimab on mortality in COVID-19–infected patients on hemodialysis (HD).

Methods: We conducted an observational retrospective study in 230 COVID-19–infected patients on HD, of whom 77 (33.5%) were administered regdanvimab alone or in combination with dexamethasone or remdesivir during hospitalization (regdanvimab group) and 153 patients (66.5%) were not (no regdanvimab group). The primary outcome was in-hospital mortality. We compared mortality rates according to the use of regdanvimab and investigated the factors associated with mortality.

Results: Fifty-nine deaths occurred during hospitalization, 49 in the no regdanvimab group (32.0%) and 10 in the regdanvimab group (13.0%), and the mortality rate was significantly higher in the no regdanvimab group than that in the regdanvimab group (p = 0.001). Multivariate Cox regression analysis showed that malignancy (p = 0.001), SPO_2 of <95% at admission (p = 0.003), and administration of antibiotics and regdanvimab (p = 0.007 and p = 0.002, respectively) were significantly associated factors with mortality.

Conclusion: Regdanvimab administration is beneficial in improving prognosis in hospitalized COVID-19 patients on HD. Considering the vulnerability to infection and high mortality of ESRD patients, regdanvimab may be considered as a therapeutic option in COVID-19 patients on HD.

Keywords: COVID-19, Renal dialysis, Mortality, Regdanvimab

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Introduction

Coronavirus disease 2019 (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread globally since December 2019. The urgent need for effective treatments has led to unprecedented research efforts, and treatment guidelines for COVID-19 are being revised and updated based on results from clinical studies that evaluated therapeutic agents and approaches [1–3]. Among therapeutic agents, regdanvimab (Regkirona, Celltrion Healthcare) is a recombinant neutralizing monoclonal antibody that received final approval in September 2021 in South Korea for the treatment of COVID-19 [4]. Early treatment with regdanvimab has been shown to reduce the severity of disease and associated hospitalization or intensive care unit (ICU) admittance in COVID-19 patients with mild-to-moderate symptoms [5,6].

Patients with end-stage renal disease (ESRD) on hemodialysis (HD) are more vulnerable to this viral epidemic due to inevitable regular visits to dialysis units and contact with susceptible patients. Moreover, those on ESRD generally have many comorbidities and are in an immunocompromised state. Previous studies have shown that patients with ESRD have a higher mortality rate compared with those of the general population [7–9]. Regdanvimab is generally considered for use in adult patients with moderate symptoms or elderly patients aged >50 years with mild symptoms and at least one underlying medical condition, including obesity, cardiovascular disease, chronic lung disease, diabetes mellitus, and chronic liver disease; patients on immunosuppressive agents; and patients with chronic kidney disease [10]. Based on these indications, regdanvimab is considered for use in ESRD patients in the current clinical setting; however, data on the usage and effectiveness of regdanvimab in ESRD patients are still lacking.

To further clarify the clinical evidence of regdanvimab use in ESRD patients, the present study aims to evaluate the real-world effectiveness of regdanvimab on mortality in COVID-19–infected patients on HD.

Methods

This study was approved by the Institutional Review Board of Hallym University Kangnam Sacred Heart Hospital (No. HKS 2021-07-013). The need to obtain informed consent was waived due to the retrospective nature of the study.

Study design and participants

We retrospectively recruited all hospitalized, COVID-19–infected patients on HD who were admitted and treated at Good Samaritan Bagae Hospital (Pyeongtaek, Republic of Korea) from December 1, 2020 to November 30, 2021. Among the 338 patients, we finally analyzed the data of 230 patients who received dexamethasone, remdesivir, and regdanvimab and excluded 108 patients who received only conservative treatment without these drugs. Of them, 153 patients did not receive regdanvimab during hospital stay and 77 patients received regdanvimab alone or in combination with dexamethasone or remdesivir (Fig. 1). The diagnosis of COVID-19 was confirmed using real-time reverse transcription-polymerase chain reaction assays using samples from the upper or lower respiratory tract.

Clinical management

All hospitalized patients received symptomatic care, including oxygen, antipyretics, and antitussive agents. Therapeutic agents including dexamethasone, antibiotics, and antiviral agents were administered to the selected patients within 1 to 2 days after admission according to hospital protocols and clinician decision.

In our center, regdanvimab was considered for patients with at least one risk factor, with a one-week duration since disease onset, and with no need for supplemental oxygen. Risk factors included obesity, cardiovascular disease, chronic lung disease, type 1 or type 2 diabetes mellitus, and chronic liver disease. In some cases, regdanvimab was considered for patients requiring low-concentrated oxygen according to the clinician's judgment. The physician explained the possible side effects of regdanvimab, and only patients who consented to its use were prescribed.

Data collection and mortality

The electronic medical records of all participating patients were reviewed. Baseline characteristics were investigated on the day when the patients were admitted to the institution after COVID-19 infection was confirmed. The clinical information of interest included age, sex, body mass index

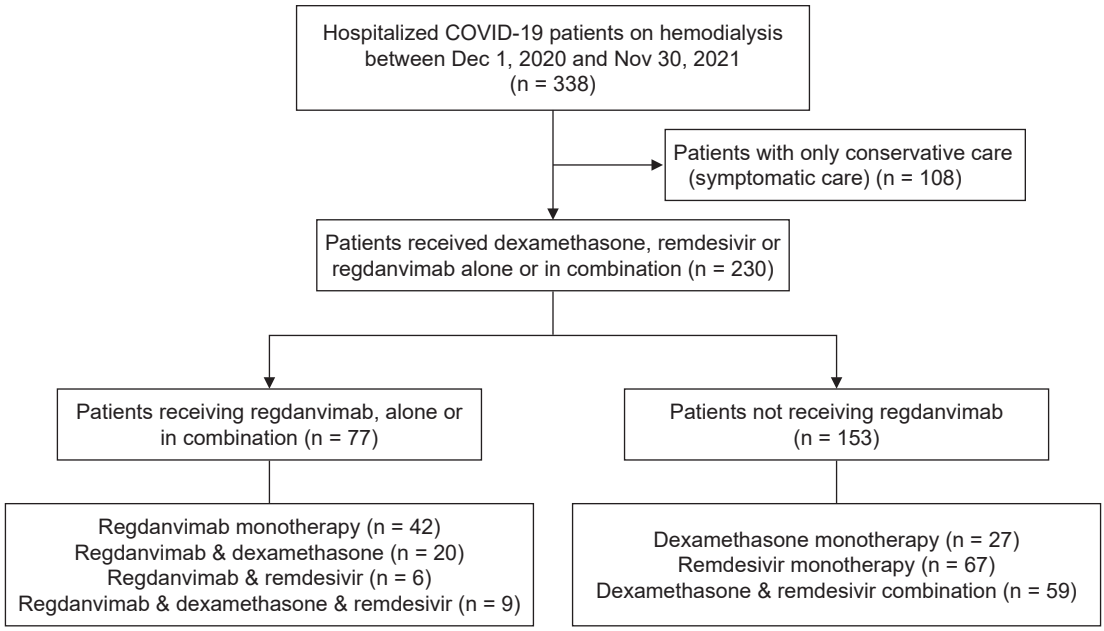

Figure 1. Flow chart of the study population. Coronavirus disease 2019 (COVID-19)-infected patients on hemodialysis who were admitted at Good Samaritan Bagae Hospital from December 1, 2020 to November 30, 2021 were recruited. Regdanvimab group was administered regdanvimab alone or in combination with dexamethasone or remdesivir during hospitalization and no regdanvimab group was not.

(BMI), underlying kidney disease, use of renin-angiotensin system blockers, type of dialysis unit before admission, underlying disease, initial symptoms, and saturation of partial pressure oxygen (SPO_2) at admission. Baseline laboratory data were also collected. Information on treatment included antiviral or antibiotic therapy, corticosteroid therapy, admission to ICU, use of mechanical ventilation (MV), use of continuous renal replacement therapy (CRRT), and oxygen supply. In-hospital mortality, defined as all-cause mortality during hospitalization for COVID-19 infection, was set as the primary endpoint, and information on the duration of hospitalization was also investigated.

Statistical analysis

Study participants were categorized into the regdanvimab group and no regdanvimab group. The t test was used for parametric estimation, and the Wilcoxon rank-sum test was for nonparametric estimation. Categorical variables were compared using the chi-square test. The Kaplan-Meier survival curve was used to determine the differences in mortality between the groups, and the statistical significance was assessed using the log-rank test. Univariate and multivariate Cox regression analyses were used to explore the factors associated with mortality. All statistical analyses were performed using IBM SPSS version 23.0 (IBM Corp.), and p-values less than 0.05 were considered statistically significant.

Results

Baseline characteristics

In total, 230 COVID-19–infected patients on HD were included in the study, of whom 77 (33.5%) were administered regdanvimab alone or in combination with dexamethasone or remdesivir during hospitalization (regdanvimab group) and 153 patients (66.5%) were not (no regdanvimab group). Table 1 shows the baseline characteristics of the two groups. The mean age was 67.9 ± 12.1 years, and 214 patients (93.0%) were aged ≥50 years. The proportion of patients aged ≥50 years was significantly higher in the regdanvimab compared with that in the no regdanvimab group (p = 0.01). Males predominated in the study population (n = 139, 60.4%) with a high proportion in both groups. There were no significant differences in demographic character-

Table 1. Comparison of baseline characteristics between the groups

Characteristic	Total	Regdanvimab group	No regdanvimab group	p-value
No. of patients	230	77	153	
Age (yr)	67.9 ± 12.1	68.2 ± 11.1	67.8 ± 12.6	0.79
Male sex	139 (60.4)	47 (61.0)	92 (60.1)	0.51
BMI (kg/m^2)	23.5 ± 4.3	23.5 ± 3.7	23.9 ± 4.9	0.61
Kidney disease				
DM	132 (57.9)	42 (54.5)	90 (58.8)	
Hypertension	67 (29.1)	25 (32.5)	42 (27.5)	
PKD	0 (0)	0 (0)	0 (0)	
Glomerulonephritis	7 (3.0)	3 (3.9)	4 (2.6)	
Unknown	22 (9.6)	6 (7.8)	16 (10.5)	
Underlying disease				
DM	132 (57.4)	42 (54.5)	90 (58.8)	0.33
Hypertension	149 (64.8)	51 (66.2)	98 (64.1)	0.41
CAOD	41 (17.8)	16 (20.8)	25 (16.3)	0.26
CHF	9 (3.9)	4 (5.2)	5 (3.3)	0.35
CVA	29 (12.6)	10 (13.0)	19 (12.4)	0.53
Arrhythmia	13 (5.7)	3 (3.9)	10 (6.5)	0.31
Malignancy	16 (7.0)	4 (5.2)	12 (7.8)	0.33
Symptom				
Fever	94 (40.9)	25 (32.5)	69 (45.1)	0.009
Cough	51 (22.2)	14 (18.2)	37 (24.2)	0.20
Sputum	35 (17.8)	11 (14.3)	24 (15.7)	0.44
Sore throat	23 (10.0)	5 (6.5)	18 (11.8)	0.12
Rhinorrhea	12 (5.2)	4 (5.2)	8 (5.2)	0.51
Dyspnea	54 (23.5)	6 (7.8)	48 (31.4)	<0.001
SPO_2 at admission <95%	24 (10.4)	2 (2.6)	22 (14.4)	0.003
Use of RASB	96 (41.7)	32 (41.6)	64 (41.8)	0.56
Hospital type				
Private clinic	75 (32.6)	23 (29.9)	52 (34.0)	
Nursing hospital	43 (18.7)	18 (23.4)	25 (16.3)	
University hospital	34 (14.8)	10 (13.0)	24 (15.7)	
Others	38 (16.5)	14 (18.2)	24 (15.7)	
Laboratory data				
WBC (×1,000/μL)	6.34 ± 3.32	5.91 ± 2.48	6.56 ± 3.66	0.16
Neutrophil (×1,000/μL)	4.71 ± 3.12	4.12 ± 2.19	4.99 ± 3.46	0.02
Hemoglobin (g/dL)	10.8 ± 1.4	10.8 ± 1.4	10.7 ± 1.4	0.59
BUN (mg/dL)	65.8 ± 28.1	55.8 ± 18.7	70.8 ± 30.6	<0.001
Creatinine (mg/dL)	9.31 ± 3.79	8.76 ± 3.72	9.58 ± 3.81	0.12
Albumin(g/dL)	3.8 ± 0.5	3.83 ± 0.59	3.72 ± 0.51	0.14
C-reactive protein (mg/L)	5.69 ± 6.04	3.56 ± 5.01	6.76 ± 6.24	<0.001
BNP (pg/mL)	590.7 ± 786.8	459.7 ± 524.3	656.7 ± 884.4	0.04

Data are expressed as number only, mean ± standard deviation, or number (%).
BMI, body mass index; BUN, blood urea nitrogen; BNP, brain natriuretic peptide; CAOD, coronary artery obstructive disease; CHF, congestive heart failure; CVA, cerebrovascular accident; DM, diabetes mellitus; PKD, polycystic kidney disease; RASB, renin-angiotensin system blockade; SPO_2, saturation of partial pressure oxygen; WBC, white blood cell.

istics and the distribution of underlying diseases between the two groups. More patients complained of dyspnea in the no regdanvimab than in the regdanvimab group, whereas there were no differences in other symptoms such as fever, cough, sputum, sore throat, and rhinorrhea. The proportion of patients whose SPO_2 was <95% at the time of admission was higher in the no regdanvimab group than in the regdanvimab group. Laboratory data showed that neutrophil count and blood urea nitrogen, C-reactive protein, and brain natriuretic peptide levels were higher in the no regdanvimab group than those in the regdanvimab group.

Information on treatment and mortality

In addition to the administration of therapeutic agents, various supportive treatments were administered to the patients (Table 2). Remdesivir was administered in 79.1% of patients in the no regdanvimab group and 19.1% of patients in the regdanvimab group. Dexamethasone was administered in 53.2% of patients in the no regdanvimab group and 37.7% of patients in the regdanvimab group. The proportions of antibiotics use rate were 83% in the no regdanvimab group and 72.7% in the regdanvimab group, which were quite high in both groups, but there was no significant difference between the groups. The proportion of patients who received oxygen, high flow oxygen, and MV was higher in the no regdanvimab group than in the regdanvimab group. More patients in the no regdanvimab group needed ICU admission during hospitalization than did patients in the regdanvimab group. The proportion of patients receiving CRRT during hospitalization was similar in both groups.

Mortality based on regdanvimab administration

Fig. 2 shows the mortality of study patients. The mean length of hospital stay was 19.3 ± 12.3 days and was significantly longer in the regdanvimab group (22.6 ± 14.4 days) than in the no regdanvimab group (17.6 ± 10.7 days) ($p = 0.009$). Fifty-nine deaths (25.7%) occurred during hospitalization, 49 in the no regdanvimab group (32.0%) and 10 in the regdanvimab group (13.0%), and the mortality rate was significantly higher in the no regdanvimab group than that in the regdanvimab group ($p = 0.001$). According to the Kaplan-Meier curve, the regdanvimab group showed a significantly better prognosis with a higher survival rate compared with that in the no regdanvimab group (log-rank $p = 0.001$) (Fig. 3).

Factors associated with mortality in COVID-19–infected patients on hemodialysis

We investigated the factors associated with mortality among COVID-19–infected patients on HD (Table 3). Univariate Cox regression analysis showed that older age ($p < 0.001$), arrhythmia ($p = 0.01$), malignancy ($p = 0.001$), SPO_2 <95% at admission ($p < 0.001$), and low serum albumin and creatinine (both $p < 0.001$) were significant risk factors, while use of renin-angiotensin-system blockers ($p = 0.04$) and administration of antibiotics and regdanvimab ($p = 0.001$ and $p = 0.002$, respectively) were associated with low mortality in these patients. Factors related to disease severity, such as high flow oxygen, MV, CRRT, and ICU care, were all significantly associated with high mortality ($p < 0.001$). Multivariate Cox regression analysis with the

Table 2. Comparison of pharmacological and supportive treatments

Treatment	Total (n = 230)	Regdanvimab group (n = 77)	No regdanvimab group (n = 153)	p-value
Dexamethasone	115 (50.0)	29 (37.7)	86 (56.2)	0.006
Remdesivir	136 (59.1)	15 (19.1)	121 (79.1)	<0.001
Antibiotics	183 (79.6)	56 (72.7)	127 (83.0)	0.05
Oxygen apply	179 (77.8)	41 (53.2)	138 (90.2)	<0.001
High flow O_2	41 (17.8)	4 (5.2)	37 (24.2)	<0.001
Mechanical ventilation	29 (12.6)	5 (12.6)	24 (15.7)	0.03
CRRT	20 (8.7)	6 (7.8)	14 (9.2)	0.47
ICU care	61 (26.5)	14 (18.2)	47 (30.7)	0.03

Data are expressed as number (%).
CRRT, continuous renal replacement therapy; ICU, intensive care unit.

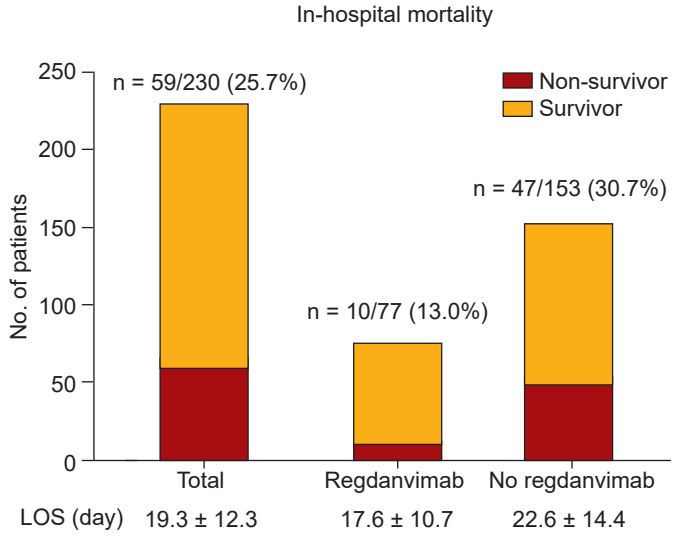

Figure 2. Mortality of study patients.
In-hospital mortality was defined as all-cause mortality during hospitalization for coronavirus disease 2019 infection.
LOS, length of hospital stay.

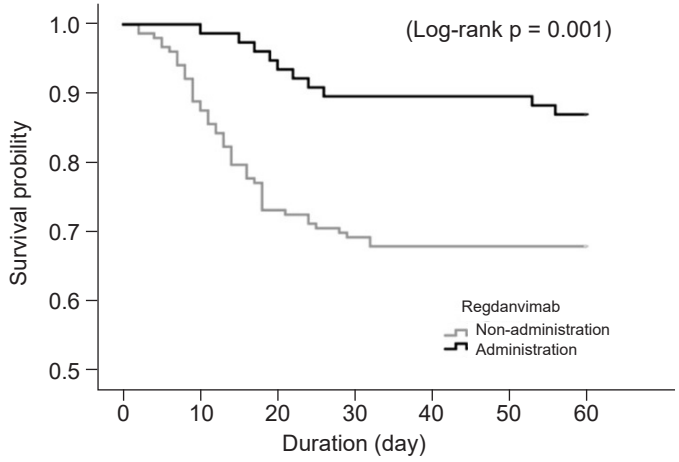

Figure 3. Kaplan-Meier curve for in-hospital mortality according to administration of regdanvimab in total study patients (n = 230).

significant variables in the univariate analysis showed that malignancy (hazard ratio [HR], 3.39; 95% confidence interval [CI], 1.62–7.11; p = 0.001), SPO_2 <95% at admission (HR, 2.83; 95% CI, 1.43–5.59; p = 0.003), MV (HR, 2.85; 95% CI, 1.21–6.75; p = 0.02), ICU care (HR, 3.03; 95% CI, 1.31–7.03; p = 0.01) and administration of antibiotics and regdanvimab (HR, 0.41; 95% CI, 0.22–0.79; p = 0.007 and HR, 0.282; 95% CI, 0.128–0.624; p = 0.002, respectively) were important factors in patient outcomes. These data suggest that regdanvimab had a beneficial effect on mortality in COVID-19–infected patients undergoing HD.

In the clinical setting, regdanvimab is generally considered in patients with mild-to-moderate disease with low oxygen demand; thus, we conducted additional analyses in patients with SPO_2 greater than 95%. The total number of included patients was 206, 131 in the no regdanvimab group and 75 in the regdanvimab group. Herein, the regdanvimab group showed a higher survival rate compared with that in the no regdanvimab group (log-rank p = 0.002) (Fig. 4). Furthermore, the use of regdanvimab was significantly associated with low mortality even after adjustment for several associated factors (HR, 0.233; 95% CI, 0.105–0.517; p < 0.001) (Table 4).

Discussion

This study found an association between mortality and regdanvimab use in hospitalized COVID-19 patients undergoing HD. The patients who received regdanvimab alone or in combination during hospitalization achieved better mortality compared with that in patients who did not. In addition, we elucidated the risk factors related to mortality, and regdanvimab showed an association with better survival even after adjusting for factors showing significant differences between groups. These findings suggest that the use of regdanvimab in COVID-19 patients on HD has a significantly favorable impact on mortality.

Along with diabetes mellitus, hypertension, and cardiovascular disease, chronic kidney disease has been reported to be associated with the severity and mortality of COVID-19 [11–13]. Specifically, patients with ESRD are immunosuppressed and usually have other chronic systemic diseases related to clinical outcomes of COVID-19 [14,15]; therefore, they have particularly higher morbidity and mortality than those of the general population [16]. Center-based HD is the main renal therapeutic modality in many countries including Korea [17]. For HD patients, the possibility of infection is high due to the confinement in an indoor environment for several hours and frequent contact with medical staff members or other patients. Therefore, during the outbreak of the COVID-19 pandemic, effective strategies were required to prevent disease transmission and improve prognosis in HD patients infected with

Table 3. Factors associated with mortality of study patients

Variable	Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age (yr)	1.05 (1.02–1.07)	<0.001	1.00 (0.99–1.07)	0.11
≥50	1.05 (0.38–2.91)	0.92		
≥60	2.26 (1.07–4.76)	0.03		
≥70	2.89 (1.66–5.04)	<0.001		
Male sex	0.89 (0.53–1.51)	0.67		
BMI	1.01 (0.92–1.11)	0.80		
RASB	0.57 (0.33–0.98)	0.04	0.94 (0.48–1.82)	0.84
DM	0.74 (0.44–1.23)	0.25		
Hypertension	0.82 (0.52–1.31)	0.41		
CAOD	1.25 (0.66–2.36)	0.49		
CHF	1.34 (0.42–4.27)	0.62		
CVA	1.54 (0.78–3.04)	0.21		
Arrhythmia	2.75 (1.25–6.06)	0.01	1.70 (0.58–4.96)	0.33
Malignancy	3.22 (1.63–6.36)	0.001	2.90 (1.27–6.59)	0.01
SPO_2 at admission (<95%)	3.63 (1.93–6.84)	<0.001	1.66 (0.78–3.50)	0.19
High flow O_2	2.97 (1.74–5.07)	<0.001	1.13 (0.56–2.29)	0.73
Mechanical ventilation	10.35 (6.10–17.58)	<0.001	2.85 (1.21–6.75)	0.02
CRRT	7.66 (4.39–13.36)	<0.001	1.51 (0.58–3.91)	0.40
ICU care	9.80 (5.55–17.29)	<0.001	3.03 (1.31–7.03)	0.01
WBC	1.04 (0.97–1.11)	0.28		
Neutrophil	1.05 (0.98–1.12)	0.16		
Hemoglobin	0.88 (0.73–1.06)	0.17		
BUN	1.00 (0.99–1.01)	0.499		
Creatinine	0.86 (0.80–0.92)	<0.001	0.95 (0.86–1.06)	0.39
Albumin	0.43 (0.27–0.69)	<0.001	0.94 (0.50–1.74)	0.84
C-reactive protein	1.03 (0.96–1.07)	0.09		
BNP	1.00 (1.00–1.00)	0.12	0.63 (0.30–1.30)	
Antibiotics	0.40 (0.24–0.69)	0.001	1.57 (0.75–3.28)	0.21
Dexamethasone	1.58 (0.94–2.65)	0.09	1.14 (0.55–2.37)	0.24
Remdesivir	1.58 (0.91–2.72)	0.10	0.32 (0.13–0.82)	0.72
Regdanvimab	0.35 (0.18–0.68)	0.002	0.95 (0.86–1.06)	0.02

BMI, body mass index; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CAOD, coronary artery obstructive disease; CHF, congestive heart failure; CI, confidence interval; CRRT, continuous renal replacement therapy; CVA, cerebrovascular accident; DM, diabetes mellitus; HR, hazard ratio; ICU, intensive care unit; RASB, renin-angiotensin system blockade; SPO_2, saturation of partial pressure oxygen; WBC, white blood cell.

COVID-19.

The COVID-19 pandemic has seen clinical development and the use of antiviral treatment at an unprecedented speed. Several potential antiviral agents have been identified that have been useful to inhibit the clinical progression and complication of COVID-19 [18]. However, many clinical trials are still required to prove the efficacy and safety of these agents; furthermore, even if some regimens are effective, most of them have not been recommended for use in HD patients. Thus, unfortunately, the development of treatment protocols and the use of potentially beneficial treatment have been delayed in HD patients infected with COVID-19, and there is still limited data for effective treatment methods in these patients.

Regdanvimab (Regkirona) is a recombinant human monoclonal immunoglobulin G1 antibody that neutralizes SARS-CoV-2 by binding to the receptor binding domain of the virus' spike protein and was effective at reducing viral

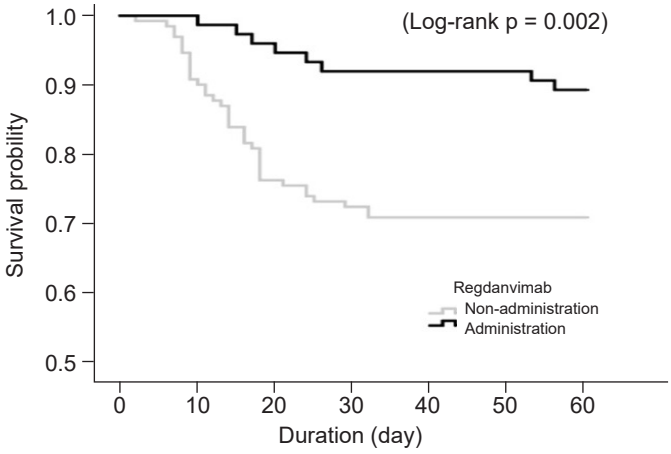

Figure 4. Kaplan-Meier curve for in-hospital mortality according to the administration of regdanvimab in patients with SPO_2 >95% (n = 206).

SPO_2, saturation of partial pressure oxygen.

load and ameliorating clinical symptoms [4]. In previous clinical trials, regdanvimab was found to be effective in reducing the progression rates to severe COVID-19 among patients with mild-to-moderate COVID-19 and shortening the clinical recovery time in patients treated with regdanvimab [19,20]. Recent retrospective studies showed that regdanvimab treatment prevented progression to severe disease; additionally, the use of regdanvimab in addition to remdesivir had a significantly favorable impact on the clinical outcomes of severe COVID-19 [21,22]. Although patients with chronic kidney disease, including those on dialysis, can undergo regdanvimab treatment, there is a lack of data on the clinical effectiveness and safety of these patients who are at high risk of suffering excess morbidity and mortality. In this observation study, we first confirmed that

Table 4. Factors associated with mortality of study patients with SPO_2 >95%

Variable	Univariate		Multivariate	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age	1.04 (1.02–1.07)	0.002	1.02 (0.99–1.06)	0.19
Male sex	1.04 (0.58–1.87)	0.90		
BMI	1.05 (0.94–1.16)	0.41		
RASB	0.51 (0.27–0.97)	0.04	0.78 (0.38–1.62)	0.50
Diabetes	0.63 (0.35–1.12)	0.11		
Hypertension	0.50 (0.45–1.48)	0.495		
CAOD	1.01 (0.45–2.26)	0.98		
CHF	1.09 (0.91–1.09)	0.91		
CVA	1.59 (0.74–3.41)	0.22		
Arrhythmia	2.42 (0.95–6.13)	0.06		
Malignancy	2.85 (1.27–6.37)	0.011	2.00 (0.82–4.85)	0.13
High flow O_2	3.84 (2.12–6.96)	<0.001	0.92 (0.43–1.97)	0.82
Mechanical ventilation	10.64 (5.83–19.40)	<0.001	3.15 (1.18–8.37)	0.02
CRRT	9.03 (4.69–17.38)	<0.001	1.49 (0.55–4.01)	0.43
ICU care	9.10 (4.89–16.92)	<0.001	3.12 (1.31–7.41)	0.01
WBC	0.87 (0.91–1.11)	0.87		
Neutrophil	1.02 (0.92–1.13)	0.67		
Hemoglobin	0.93 (0.75–1.16)	0.50		
BUN	1.00 (0.99–1.01)	0.73		
Creatinine	0.85 (0.78–0.93)	<0.001	0.92 (0.82–1.02)	0.12
Albumin	0.44 (0.25–0.75)	0.003	0.74 (0.40–1.38)	0.34
C-reactive protein	1.03 (0.98–1.07)	0.21		
BNP	1.00 (1.00–1.00)	0.16		
Antibiotics	0.40 (0.22–0.73)	0.003	0.65 (0.30–1.42)	0.28
Dexamethasone	1.24 (0.70–2.22)	0.46	1.02 (0.47–2.23)	0.96
Remdesivir	1.55 (0.84–2.83)	0.16	0.97 (0.42–2.27)	0.95
Regdanvimab	0.32 (0.15–0.69)	0.003	0.27 (0.10–0.75)	0.01

BMI, body mass index; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CAOD, coronary artery obstructive disease; CHF, congestive heart failure; CI, confidence interval; CRRT, continuous renal replacement therapy; CVA, cerebrovascular accident; HR, hazard ratio; ICU, intensive care unit; RASB, renin-angiotensin system blockade; SPO_2, saturation of partial pressure oxygen; WBC, white blood cell.

regdanvimab administration (alone or in combination) for the treatment of HD patients infected by COVID-19 would be beneficial in improving prognosis.

We further evaluated the factors associated with the mortality of HD patients infected with COVID-19. Higher age is the main determinant of increased risk of infection and mortality caused by COVID-19 [23,24]. Similar to previous results, we also found a significant association between age and patient outcomes, with a 2.3-fold increase in mortality in patients aged ≥60 years and a 2.9-fold increase in mortality in patients aged ≥70 years. In addition, the indication for regdanimab is the presence of mild disease, age ≥50 years, and the presence of at least one risk factor; in our study, significant survival benefit effects were shown in patients aged ≥60 years. Furthermore, several studies showed that preexisting comorbidities, such as hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, chronic obstructive pulmonary disease, and history of cardiac diseases, were associated with an increased risk of COVID-19-related mortality [25–29]. This study showed that arrhythmia and malignancy in the study patients were significantly associated with increased mortality. Patients with HD are often elderly and have multiple comorbidities identified as risk factors for COVID-19–related mortality; thus, rapid interventions with effective treatments are important to improve the prognosis. Despite the viral origin, antibiotics are frequently prescribed to patients with COVID-19. The rationale for antibiotic treatment in these patients seems to be based on the experience with bacterial superinfection in hospitalized patients. In our study, the proportion of patients receiving antibiotics with other treatment agents was 79.6% without a significant difference between the two groups; the use of antibiotics was significantly associated with low mortality. Previous studies showed that the prevalence of bacterial co-infection and secondary infection in patients with COVID-19 is relatively low (3.5% and 14.3%, respectively) [30], and over-prescribing of antibiotics in these patients could result in increased antimicrobial resistance [31,32]. Therefore, further studies are needed to improve the appropriateness of antibiotics use in these patients.

This study has some limitations. First, being a retrospective observational study, the study design has inherent biases such as selection and confounding biases, and unmeasured confounders might have affected the observed results. As an example, residual renal function is related not only to the prognosis of ESRD patients but also to the pharmacodynamics and pharmacokinetics, so it could be an important factor in a study related to drug effect. However, data on the residual renal function of study patients were not initially investigated, so we could not analyze by including the data on them. Second, information on the safety of regdanvimab in ESRD patients is still lacking because we could not investigate the occurrence of side effects and adverse events in study patients due to incomplete medical records. Third, we could not study the impact of regdanvimab on the disease progression as assessed by the need for MV, transfer to the ICU, and receipt of extracorporeal membrane oxygenation during hospital admission. Further studies with larger samples and prospective designs are required to consider regdanvimab as a safe and potential agent for ESRD patients infected with COVID-19. Finally, we enrolled patients before the Delta (the 4th variant of concern) and Omicron variant (the 5th variant of concern) became dominant. In South Korea, the Delta variant was first identified in the local community in May 2021 and became predominant in October 2021. This study was conducted with patients who were admitted to the institution from 1 December 2020 to 30 November 2021. Therefore, it is assumed that Delta and Omicron were not the predominant variants during the study period. Since the effectiveness of antiviral agents may differ depending on the variant, further studies on the individual subtypes of SARS-CoV-2 are required. Despite these limitations, the current findings have important clinical implications; this study is the first one evaluating the effect of regdanvimab on COVID-19 infection in patients on HD who were, thus far. limited from using this potentially beneficial treatment due to the lack of data.

In conclusion, our results showed that regdanvimab administration was beneficial in improving prognosis in hospitalized COVID-19 patients on HD. Considering the vulnerability to infection and high mortality of ESRD patients, regdanvimab may be considered as a therapeutic option in COVID-19 patients on HD.

Conflicts of interest

All authors have no conflicts of interest to declare.

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Data sharing statement

The data presented in this study are available on request from the corresponding author.

Authors' contributions

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Formal analysis: EK, JK, AC
Funding acquision: HCP
Investigation, Resources: SJY, SY
Methodology, Validation: EK, DHK, AC
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