

Effectiveness and safety of regdanvimab in patients with mild-to-moderate COVID-19: A retrospective cohort study

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Article

Keywords: regdanvimab, COVID-19, disease aggravation

Posted Date: September 21st, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-846378/v1>

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Abstract

Regdanvimab has decreased the time to clinical recovery from coronavirus disease 2019 (COVID-19) and lowered the rate of oxygen therapy according to the results from Phase 2 randomized controlled trial. More information is needed about the effects and safety of regdanvimab. We analyzed the medical records of patients with high-risk mild or moderate COVID-19 being admitted to Busan Medical Center between December 1, 2020, and April 16, 2021. A propensity score (PS) matched analysis was conducted to compare patients with and without regdanvimab. The primary outcome was in-hospital death or disease aggravation. Among 1,617 selected patients, 970 (60.0%) were indicated for regdanvimab. Among a 1:1 PS-matched cohort of 377 patients each treated with and without regdanvimab, regdanvimab significantly reduced the primary endpoint (odds ratio [OR], 0.194; 95% confidence interval [CI], 0.112–0.320; $p < 0.001$). Regdanvimab was associated with a significantly lower risk of disease aggravation without increasing adverse reactions.

Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified at the end of 2019 as the cause of the outbreak of acute respiratory syndrome in Wuhan, Hubei Province, China.¹ Thereafter, it spread rapidly around the world, causing a pandemic, and was named coronavirus disease 2019 (COVID-19).² Vaccination against SARS-CoV-2 began in several countries from mid-December 2020, and by ~ 7 months later, nearly a quarter of the global population had received at least one dose of vaccine.³ However vaccine inequity is significant among nations, and only about 1% of the population in low-income countries have been vaccinated with even one dose.³ Globally, 2.6 million people per week contract COVID-19, and the number of new deaths, although declining, is still > 50,000 per week.⁴ As of July 9, 2021, the global cumulative numbers of persons infected with COVID-19 and consequent deaths have exceeded 185 and 4 million, respectively.⁵ Various vaccines and treatments are being developed to overcome COVID-19, but more therapeutic strategies are needed. Furthermore, viruses mutate over time, which seems to affect viral transmission and disease severity, as well as vaccine and therapeutic efficacy.⁶ The only drugs recommended by the WHO for treating patients with COVID-19 are corticosteroids and interleukin-6 receptor blockers (tocilizumab or sarilumab) in severe or critical patients.⁷ Among antivirals, remdesivir has been approved by the U.S. Food and Drug Administration (FDA) for hospitalized patients with COVID-19 who require supplemental oxygen.⁸

Monoclonal antibodies (mAbs) targeting specific regions of viral surface proteins should be promising treatments against infectious diseases,^{9,10} and they are therapeutically effective against several viruses.^{11,12} Among the anti-SARS-CoV-2 mAbs for the treating COVID-19, combination therapies of bamlanivimab/etesevimab and casirivimab/imdevimab have received emergency use authorization (EUA) from the FDA for outpatients with mild to moderate COVID-19 at high risk and they are recommended by the National Institutes of Health (NIH).⁸

Regdanvimab (CT-P59) is a recombinant neutralizing mAb constructed from the blood of convalescing patients with COVID-19, and it potently neutralizes the receptor-binding site of the SARS-CoV-2 spike protein as an antigen target.¹³ Results from a Phase 2/3 randomized, double-blind, placebo-controlled clinical trial of outpatients with mild to moderate SARS-CoV-2 infection found that regdanvimab shortened the time to conversion to a negative real-time quantitative reverse transcriptase polymerase chain reaction (RT-PCR) result and clinical recovery without causing serious side effects or death, and lowered rates of oxygen therapy.¹⁴ Regdanvimab received product approval based on these results on February 5, 2021, under the condition of submitting the results of the phase 3 clinical trial thereafter, and it became available to improve clinical symptoms in patients aged ≥ 18 years at high-risk mild or moderate COVID-19.¹⁵ High-risk is defined as age ≥ 60 years, or having ≥ 1 underlying disease such as cardiovascular or chronic respiratory diseases including asthma, hypertension, or diabetes, and moderate refers to patients with pneumonia.¹⁶ On March 26, 2021, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) concluded that regdanvimab could be used to treat adult patients with COVID-19 who do not require supplemental oxygen but are at high risk of progression to severity.¹⁷

No drugs had been approved in Korea for treating mild to moderate COVID-19 until the conditional approval of regdanvimab.¹⁸ Therefore, regdanvimab is presently the only agent available in Korea that could prevent progression in patients at high-risk mild to moderate COVID-19. However, since the results of the phase 3 clinical trial have not yet been published and accumulated data are scant, the basis for judgment regarding treatment selection in routine clinical practice is insufficient.

Busan Medical Center (BMC) in Busan, the second largest city in Korea, is a currently operating, dedicated COVID-19 treatment facility. As of April 16, 2021, ~ 3,000 inpatients have been treated, and regdanvimab has been administered to > 400 patients since its approval. This study aimed to evaluate the effectiveness and safety of regdanvimab administered to patients at high-risk mild to moderate COVID-19 in real-world clinical practice. Given the lack of accumulated data about regdanvimab, we hope that the present results will serve as a meaningful basis for drug selection to treat patients with COVID-19.

Results

Baseline patient characteristics

Among 1,617 patients with COVID-19 who were admitted during the study period, 970 (60.0%) were eligible for regdanvimab administration. These were assigned to receive treatment with ($n = 377$; 38.9%) or without ($n = 593$; 61.1%) regdanvimab (Figure 1). Some immobile patients ($n = 73$) in the untreated group with missing height and weight records were excluded from analysis. Table 1 shows the baseline characteristics of the 897 patients. Patients in group without regdanvimab were older (median age 65 [IQR, 57–75] vs. 61 [53–68] years, $p < 0.001$), but sex did not significantly differ ($p = 0.220$). They had a lower BMI (23.5 (21.5–25.7) vs. 23.9 (22.3–26.1), $p = 0.003$), and a higher proportion of comorbid cardiovascular (73.9% vs. 26.1%, $p < 0.001$) and chronic lung (78.9% vs. 21.1%, $p = 0.007$) diseases. The proportion of patients with moderate COVID-19 (with pneumonia), was also higher in the untreated group (54.1%

vs. 45.9%, $p = 0.049$). Other comorbidities (diabetes mellitus, hypertension, chronic kidney disease, and chronic liver disease) and co-medications (ACEIs/ARBs, statins, aspirin, and immunomodulators) did not significantly differ between the two groups.

Propensity-matched cohort characteristics

We created a PS-matched cohort of 754 patients, among whom, 377 were treated with regdanvimab and 377 were not. Demographics and comorbidities did not significantly differ between the PS-matched groups (Table 1). Among the co-medications that were not included in the matching variables, aspirin was prescribed to more patients in the regdanvimab group (Table 1). Supplemental Figure 1 shows the distributions of covariates before and after PS matching. Differences in baseline characteristics were attenuated in the matched, compared with the unmatched cohort (Supplemental Figure 2).

Patients in the PS-matched cohort who were treated with regdanvimab had significantly lower CRP (0.4 [0.4–1.8] vs. 0.7 [0.4–2.7], $p < 0.001$), LDH (206.0 [180.8–240.0] vs. 216.0 [90.5–257.0], $p = 0.011$), and ferritin (169.0 [100.5–307.0] vs. 221.5 [124.3–378.3], $p = 0.048$) values, whereas D-dimer, troponin I, and creatine kinase values did not significantly differ (Table 2). Supplemental Table 1 shows details of the missing baseline laboratory data.

Clinical outcomes of propensity score-matched cohort

Table 3 shows the clinical outcomes in the PS-matched cohort. The primary endpoint (composite of death or disease aggravation) was reached by 19 (5%) and 81 (21.5%) patients treated with and without regdanvimab, respectively. Regdanvimab was associated with a significant reduction in the primary endpoint in univariate (OR, 0.194; 95% CI, 0.112–0.320; $p < 0.001$) and multivariable-adjusted analyses (OR, 0.169; 95% CI, 0.095–0.287; $p < 0.001$) (Supplemental Table 2). The secondary outcome, length of hospital stay, was shorter in the group treated with, than without regdanvimab (11 (11–11) vs. 12 (11–15), $p < 0.001$). The hematological adverse reactions of white blood cell abnormalities, thrombocytopenia, and lymphocytopenia were more frequent in the group that were not treated with regdanvimab, but other investigated adverse reactions did not significantly differ between the groups (Table 3). The findings of multivariable-adjusted logistic regression analyses associated age (OR, 1.049, 95% CI 1.028–1.072, $p < 0.001$), male sex (OR, 2.209, 95% CI 1.351–3.645, $p = 0.002$), BMI (OR, 1.115, 95% CI 1.040–1.196, $p = 0.002$), and concurrent pneumonia (OR, 4.743, 95% CI 2.883–7.986, $p < 0.001$) with increased odds of reaching the primary endpoint (Figure 2A).

Multivariable adjustment in the overall cohort

Regdanvimab was significantly associated with a reduction in the primary endpoint in the overall cohort in the multivariable-adjusted analysis (OR, 0.148; 95% CI, 0.084–0.247; $p < 0.001$) (Supplemental Table 2). Other factors associated with increased odds of reaching the primary endpoint were age (OR, 1.056; 95% CI, 1.038–1.076; $p < 0.001$), male sex (OR, 1.588; 95% CI, 1.041–2.428; $p = 0.032$), BMI (OR, 1.076; 95% CI, 1.015–1.141; $p = 0.014$), chronic kidney disease (OR, 5.178; 95% CI, 1.151–25.582; $p = 0.038$), and concurrent pneumonia (OR, 4.807; 95% CI, 3.165–7.403; $p < 0.001$) (Figure 2B). Supplemental Table 2 shows the association between regdanvimab and the primary endpoint among the analytical methods in the PS-matched and overall cohorts. The influencing factors in multivariable and stepwise multivariable logistic regression analyses including all covariates were consistent regardless of the analytical method.

Discussion

This retrospective analysis evaluated the effects and safety of regdanvimab in a PS-matched cohort of patients with mild-to-moderate COVID-19. Regdanvimab reduced disease aggravation by ~ 83% in the PS-matched cohort compared with conventional treatment, without increasing adverse outcomes. The results were consistent across analytical or matching methods, and disease aggravation in the overall cohort was consistently reduced by ~ 85%. In terms of mortality, none of the patients died in the PS-matched cohort, but in the overall cohort, 17 (3.3%) of 520 without regdanvimab treatment died compared with none in the regdanvimab group (Supplemental Table 3).

The results from part one of a phase 2/3 randomized clinical trial of patients with mild-to-moderate COVID-19 found that regdanvimab 40 mg/kg reduced the need for hospitalization or oxygen therapy by > 50% compared with placebo (4.0% vs. 8.7%). It was more effective in patients with moderate COVID-19 (6.5% vs. 15.8%) and even more effective in moderate COVID-19 aged ≥ 50 years (7.5% vs. 23.7%).¹⁴ Although the results of the phase 3 clinical trial of regdanvimab have not yet been published, press releases state that it reduces the incidence of hospitalization or death by 72% among high-risk patients and by 70% in all patients.¹⁹ Here, we presumed that the regdanvimab effect on preventing the disease aggravation was somewhat greater because we targeted patients with high-risk mild or moderate COVID-19 who were indicated for regdanvimab.

The present results are comparable to those of other studies of neutralizing mAbs. Although some administration protocols differed, the results of the phase 3 BLAZE-1 study showed that bamlanivimab 700 mg and etesevimab 1,400 mg reduced COVID-19 related hospitalization or death by 87% compared with a placebo (0.8% vs. 6%, $p < 0.0001$).^{20,21} Moreover, four patients given a placebo died, whereas no-one given bamlanivimab and etesevimab died ($p = 0.01$).^{20,21} The number of medically attended visits was reduced by 49% by neutralizing antibody mixture comprising 1,200 mg each of casirivimab and imdevimab compared with a placebo (3% vs. 6%).²²

Fewer adverse reactions occurred in the group with, than without regdanvimab, which is presumably because more alternative therapeutic agents were administered to the latter group (Supplemental Table 4).

Other than regdanvimab, factors affecting disease aggravation were identified as concurrent pneumonia, male sex, increased BMI, and advanced age. Pneumonia is a criterion for judging moderate disease, and age is an established risk factor for COVID-19; therefore, age \geq 60 years was included in the criteria for regdanvimab administration. Obesity is not included in the Korean regdanvimab indication, but it is in the EMA advice. Male sex was associated with a distinctly unfavorable disease prognosis. Others have noted similar results,^{23–26} and perhaps male sex should be considered as a risk factor for COVID-19. Other drugs that might have affected COVID-19, such as ACEIs/ARBs, statins, aspirin, and immunomodulators, did not significantly differ in this study.

This study has some limitations. We reduced bias in the observational studies using PS-matched and multivariable logistic regression analyses, but the possibility that unmeasured confounding factors might remain cannot be ruled out. Other factors that might affect outcomes, such as insurance type and income level, were not included. The entire cost of COVID-19 treatment is covered by the Korean government, so insurance type or income level was not considered as an influencing factor in the present study. However, these should be considered an important factor in other countries. Vaccination was not included in the investigation because no breakthrough infection occurred after vaccination among our study participants. In addition, since only a few mutant virus infections were confirmed, this study did not consider them as influencing factors and did not include them. However, breakthrough infection is also likely to increase as rates of vaccination and mutant virus infection increase, so these might also become important factors affecting treatment outcomes. The secondary outcomes were somewhat ambiguous. In terms of hospitalization, since BMC manages non-critical COVID-19 patients and some patients suffering from deterioration involve in transfer to a tertiary hospital rather than stay, the length of the hospital stay in BMC might partly reflect deterioration of the patient's clinical status. In addition, discharge was delayed for some patients due to reasons unrelated to the progress of COVID-19, such as those who were guardians of pediatric patients or had unrelated comorbidities. Therefore, the length of the hospital stay might be difficult to equate with the clinical status of patients. Unlike other countries, patients diagnosed with COVID-19 are mostly hospitalized regardless of severity in Korea. Therefore the meaning of hospitalization or length of the hospital stay may differ from that in other countries. The adverse reactions of fever or systemic pain, injection site inflammation, hypersensitivity, and gastrointestinal toxicity were retrospectively identified based on EMR records; thus, minor symptoms might have been omitted or not closely followed up. Other adverse events identified based on laboratory data only included those during hospitalization, and not for longer periods.

Despite these limitations, the present findings have several important implications. Regdanvimab is the only neutralizing mAb against SARS-CoV-2 available in Korea, and it has shown significant clinical effectiveness as a single agent. However, the results of the phase 3 clinical trials await publication, and sufficient evidence for its routine clinical application is lacking. We hope that the real-world evidence provided herein, along with the results of the phase 3 clinical trials, will serve as a basis for effectively treating COVID-19. Controlling the transition to severe disease will prevent the collapse of medical systems in a pandemic situation where large number of patients are affected, and will also have important economic implications. The use of therapeutics cannot be overlooked, as COVID-19 continues to thrive despite vaccination.

Studies on the therapeutic effects of neutralizing antibodies, including regdanvimab, on mutated variants are currently in progress.^{27–29} Further studies of the regdanvimab effectiveness in actual clinical practice are needed on breakthrough or mutant virus infection.

Conclusion

Regdanvimab was significantly associated with lower odds of disease aggravation in 754 PS-matched patients at a 1:1 ratio who were administered with regdanvimab or not (n = 377 each; OR, 0.169; 95% CI, 0.095–0.289; p < 0.001) without increasing adverse reactions.

Declarations

ACKNOWLEDGMENTS

According to the national COVID-19 response policy, and under the management of the Korea Disease Control and Prevention Agency (KDCA), Celltrion (Incheon, Korea) supplied Regkirona® Inj. (regdanvimab 960 mg/16 mL vial) free of charge to this hospital designated for COVID-19 treatment. This study did not receive research funding, and the results are not associated with Celltrion.

AUTHOR CONTRIBUTIONS

S.P. - designed the study, processed, interpreted, accessed and verified the data, performed data analysis, and drafted the manuscript. N.K.J. - designed the study, performed data analysis, and critically revised the manuscript. D.W.K. - acquired the data and critically revised the manuscript. M.P. - acquired the data and critically revised the manuscript. J.H. - conceived and helped with study design, acquired, interpreted, accessed and verified the data, and critically revised the manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

Methods

Patient population and data elements

This observational study retrospectively analyzed the medical records of adult patients (aged ≥ 18 years) with COVID-19 (confirmed by RT-PCR) who were admitted to BMC between December 1, 2020, and April 16, 2021. Each patient followed up until death or discharge. The study period ended on May 14, 2021, allowing for the last date of discharge in all patients. The patients with high-risk mild to moderate COVID-19 were extracted and assigned to groups that were treated or not with regdanvimab. Since regdanvimab was supplied and administered at BMC from February 19, 2021, all patients given regdanvimab were hospitalized after that date. The patients who were not treated with regdanvimab were admitted before February 19, 2021, and some who were hospitalized when regdanvimab became accessible refused to be treated with it.

Baseline characteristics including age, sex, body mass index (BMI), comorbidities, and co-medications were analyzed. Comorbidities consisted of diabetes mellitus, hypertension, and cardiovascular, chronic lung, chronic kidney, and chronic liver diseases, as well as pneumonia, which is an indicator of moderate COVID-19. Co-medications included those that were presumed to affect COVID-19 treatment in previous studies, and those administered to treat comorbidities. These were classified as angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs),^{30,31} statins,^{32,33} aspirin,^{34,35} and immunomodulators.^{36,37} Immunomodulators include immunosuppressants and corticosteroids.

Several laboratory parameters at baseline that were also collected from electronic medical records (EMRs), included complete blood cell count (CBC), electrolytes, renal function, hepatic panel, C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer, troponin I, ferritin, and creatine kinase.

The Institutional Review Board (IRB) of Pusan National University approved this study (PNU IRB/2021_66_HR) and waived the requirement for informed consent. The data used in this study were anonymized after extracting patient data from the institution's electronic medical records and did not contain any personally identifiable information.

Study exposure

The exposure in this study was regdanvimab. Regdanvimab administration was also identified in the EMRs. Regdanvimab was administered at the recommended dose of a single intravenous infusion of 40 mg/kg. Remdesivir, hydroxychloroquine, azithromycin, lopinavir/ritonavir, and corticosteroids were evaluated as other treatment exposures of interest.

Study outcomes

The primary outcome was a composite of in-hospital death or disease aggravation. Disease aggravation indicators included the need for oxygen therapy (low- or high-flow oxygen therapy, and mechanical ventilation) or transfer to a tertiary hospital for further invasive treatment. The secondary outcomes were length of hospital stay (days) and adverse reactions including fever or systemic pain, injection site reaction, hypersensitivity, and gastrointestinal, hematological, renal, and hepatic toxicity.

Statistical analysis

We assessed differences in demographic characteristics, baseline clinical characteristics, and co-medications between the groups. Summary statistics are presented as medians with interquartile ranges (IQRs) for continuous variables, and numbers and percentages for categorical variables. Between-group differences were examined using Student t-tests and chi-squared tests, as appropriate. The low accuracy of chi-squared tests was compensated for using Fisher exact tests.

Although the study was limited to patients suitable for regdanvimab administration, the baseline characteristics between the regdanvimab treated and untreated groups differed. Therefore, we balanced measured covariates by estimating propensity scores (PS) of regdanvimab administration using a multivariable logistic regression model, adjusted for the variables of age, sex, BMI, comorbidities, and disease severity. Propensity scores were matched using the optimal method without designation of a caliper to prevent omission of the group treated with regdanvimab, and the results were confirmed. All baseline variables in the PS-matched cohort were descriptively analyzed.

Differences in outcomes between groups with and without (reference) regdanvimab therapy in the PS-matched cohort and whether the estimated effect of regdanvimab remained consistent in the overall cohort were determined by multivariable logistic regression analyses. Variables in the multivariable analyses that affect the prognosis of COVID-19 were included as risk factors in the regdanvimab dosing criteria.¹⁷ Co-medications were included, and sex was added based on recent findings.^{24,38}

Missing data

Among the 970 patients included in the study, 73 (7.5%) had no BMI information and were excluded from analyses. Some of the 897 patients included in the analysis had missing baseline laboratory values, and Table 1 shows laboratory results after excluding them.

All data were statistically using R version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria), and values with $P < 0.05$ were considered significant.

DATA AVAILABILITY

Anonymized data will be made available upon request to the corresponding author. These cannot be made publicly available given institutional restrictions.

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Tables

Table 1. Baseline characteristics in unmatched and propensity score matched cohorts of patients.

	Unmatched (n=897)				Matched (n=754)			
	No Regdanvimab (n=520, 58.0%)	Regdanvimab (n=377, 42.0%)	p value	SMD	No Regdanvimab (n=377)	Regdanvimab (n=377)	p value	SMD
Demographics								
Age (years)	65 (57-75)	61 (53-68)	<0.001	0.343	62 (55-69)	61 (53-68)	Matched	0.239 0.086
Sex			0.220	0.083			Matched	0.825 0.016
Male	205 (55.6%)	164 (44.4%)			161 (49.5%)	164 (50.5%)		
Female	315 (59.7%)	213 (40.3%)			216 (50.4%)	213 (49.7%)		
BMI (kg/m ²)	23.5 (21.5-25.7)	23.9 (22.3-26.1)	0.003	0.198	24.0 (22.1-26.3)	23.9 (22.3-26.1)	Matched	0.465 0.053
Comorbidities								
Cardiovascular disease	82 (73.9%)	29 (26.1%)	<0.001	0.253	27 (48.2%)	29 (51.8%)	Matched	0.781 0.020
Chronic lung disease	30 (78.9%)	8 (21.1%)	0.007	0.188	6 (42.9%)	8 (57.1%)	Matched	0.590 0.039
Diabetes mellitus	128 (59.8%)	86 (40.2%)	0.532	0.042	83 (49.1%)	86 (50.9%)	Matched	0.793 0.019
Hypertension	236 (61.0%)	151 (39.0%)	0.112	0.108	154 (50.5%)	151 (49.5%)	Matched	0.824 0.016
Chronic kidney disease	12 (75.0%)	4 (25.0%)	0.164	0.097	3 (42.9%)	4 (57.1%)	Matched	1.000* 0.028
Chronic liver disease	14 (50.0%)	14 (50.0%)	0.385	0.058	11 (44.0%)	14 (56.0%)	Matched	0.542 0.044
Pneumonia	199 (54.1%)	169 (45.9%)	0.049	0.133	161 (48.8%)	169 (51.2%)	Matched	0.557 0.043
Co-medications								
ACEIs/ARBs	144 (55.2%)	117 (44.8%)	0.277	0.073	97 (45.3%)	117 (54.7%)		0.106 0.118
Statins	148 (58.5%)	105 (41.5%)	0.841	0.014	92 (46.7%)	105 (53.3%)		0.281 0.079
Aspirin	59 (57.3%)	44 (42.7%)	0.880	0.010	27 (38.0%)	44 (62.0%)		0.034 0.155
Immunomodulators	6 (50.0%)	6 (50.0%)	0.573	0.038	5 (45.5%)	6 (54.5%)		0.761 0.022

Data are presented as *n* (%) or medians (IQR). Continuous variables were analyzed using Student t-tests. Categorical variables were analyzed using chi-squared tests. Chronic kidney disease in matched cohorts was analyzed using Fisher exact tests.

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; BMI, body mass index; SMD, standardized mean difference. * Fisher exact test.

Table 2. Baseline laboratory data in propensity score-matched cohort.

	No Regdanvimab (n=377)	Regdanvimab (n=377)	p value	SMD
WBC (10 ³ /microL)	4.6 (3.7-5.9)	4.6 (3.7-5.9)	0.484	0.051
Hemoglobin (g/dL)	13.5 (12.5-14.3)	13.5 (12.5-14.4)	0.444	0.056
Platelet count (10 ³ /microL)	187.0 (152.0-235.5)	180.0 (149.0-216.0)	0.005	0.205
Absolute neutrophil count (/microL)	2916 (2154-3926)	2834 (2037-3982)	0.142	0.107
Absolute lymphocyte count (/microL)	1058 (790-1431)	1206 (928-1564)	<0.001	0.243
Na (mmol/L)	139.0 (137.0-140.5)	139.0 (138.0-141.0)	0.002	0.224
K (mmol/L)	4.0 (3.8-4.2)	4.0 (3.7-4.2)	0.306	0.075
Creatinine (mg/dL)	0.7 (0.6-0.9)	0.7 (0.6-0.9)	0.703	0.028
GFR (mL/min)	97.2 (79.9-110.8)	95.8 (80.0-110.6)	0.626	0.036
AST (IU/L)	28.0 (22.0-38.0)	26.0 (21.0-32.0)	0.202	0.093
ALT (IU/L)	23.0 (17.0-36.0)	23.0 (17.0-34.0)	0.488	0.051
Total bilirubin (mg/dL)	0.5 (0.4-0.7)	0.6 (0.4-0.7)	0.847	0.014
CRP (mg/L)	0.7 (0.4-2.7)	0.4 (0.4-1.8)	<0.001	0.255
LDH (units/L)	216.0 (190.5-257.0)	206.0 (180.8-240.0)	0.011	0.185
D-dimer (ng/mL)	138.5 (95.8-224.5)	146.0 (102.8-208.0)	0.101	0.125
Troponin I (ng/L)	0.004 (0.002-0.009)	0.004 (0.003-0.006)	0.860	0.014
Ferritin (mcg/L)	221.5 (124.3-378.3)	169.0 (100.5-307.0)	0.048	0.158
Creatine kinase (units/L)	83.0 (58.0-123.2)	79.0 (55.3-116.0)	0.800	0.019

Data are presented as medians (IQR). Variables were analyzed using Student t-tests. ALT, alanine transaminase; AST, aspartate transaminase; CRP, C-reactive protein; GFR, glomerular filtration rate; LDH, lactate dehydrogenase; SMD, standardized mean difference, WBC, white blood cells.

Table 3. Clinical outcomes in propensity score-matched cohort.

	No Regdanvimab (n=377)	Regdanvimab (n=377)	p value
Primary endpoint	81 (21.5%)	19 (5.0%)	<0.001
Length of hospital stay (day)	12 (11-15)	11 (11-11)	<0.001
Adverse reactions			
Fever or systemic pain	62 (16.4%)	57 (15.1%)	0.617
Injection site reaction	-	-	-
Hypersensitivity	1 (0.3%)	1 (0.3%)	1.000*
Gastrointestinal toxicity	13 (3.4%)	6 (1.6%)	0.104
Abnormality of white blood cell			<0.001
Elevation (>10×10 ³ /microL)	45 (11.9%)	19 (5.0%)	
Decrease (<4×10 ³ /microL)	56 (14.9%)	29 (7.7%)	
Decrease in hemoglobin (<10.0 g/dL)	10 (2.7%)	5 (1.3%)	0.192
Decrease in platelet (<130×10 ³ /microL)	22 (5.8%)	9 (2.4%)	0.017
Decrease in ANC			0.188*
Mild (1000~1500/microL)	31 (8.2%)	23 (6.1%)	
Moderate (500~1000/microL)	12 (3.2%)	6 (1.6%)	
Severe (<500/microL)	1 (0.3%)	0 (0.0%)	
Decrease in ALC (<800/microL)	45 (11.9%)	11 (2.9%)	<0.001
Abnormality of serum sodium			0.373*
Elevation (>150 mmol/L)	0 (0.0%)	0 (0.0%)	
Decrease (<130 mmol/L)	4 (1.1%)	1 (0.3%)	
Abnormality of serum potassium			0.342*
Elevation (>5.5 mmol/L)	3 (0.8%)	0 (0.0%)	
Decrease (<3 mmol/L)	2 (0.5%)	2 (0.5%)	
Renal toxicity	6 (1.6%)	7 (1.9%)	0.780
Liver toxicity	12 (3.2%)	5 (1.3%)	0.086

Data are presented as *n* (%) or median (IQR). Continuous and categorical variables were analyzed using Student's t-tests and chi-squared tests, respectively. *Categorical variables also analyzed by Fisher exact tests to compensate for low accuracy of chi-squared tests.

Figures

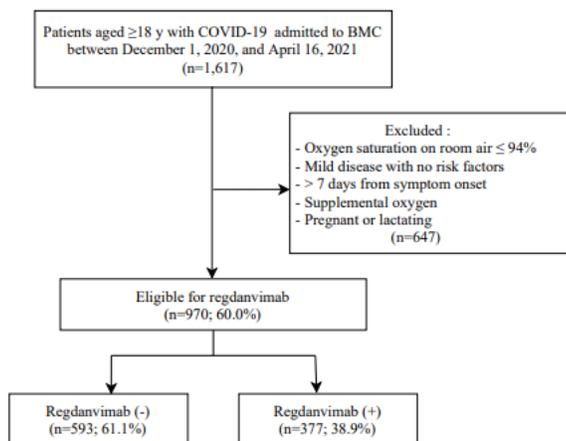
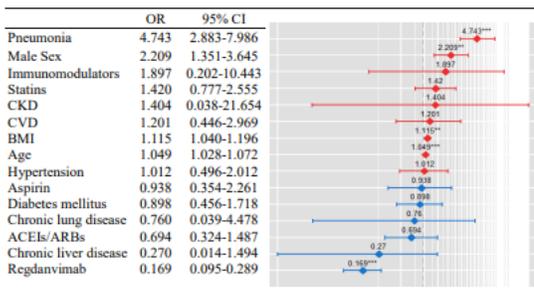


Figure 1

Among 1,617 patients with COVID-19 who were admitted during the study period, 970 (60.0%) were eligible for regdanvimab administration. These were assigned to receive treatment with (n = 377; 38.9%) or without (n = 593; 61.1%) regdanvimab.

A Propensity score-matched cohort.



B Overall cohort

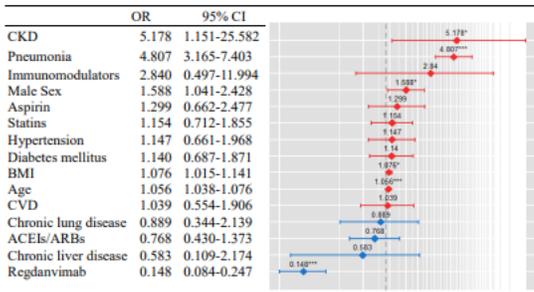


Figure 2

The findings of multivariable-adjusted logistic regression analyses associated age (OR, 1.049, 95% CI 1.028-1.072, $p < 0.001$), male sex (OR, 2.209, 95% CI 1.351-3.645, $p = 0.002$), BMI (OR, 1.115, 95% CI 1.040-1.196, $p = 0.002$), and concurrent pneumonia (OR, 4.743, 95% CI 2.883-7.986, $p < 0.001$) with increased odds of reaching the primary endpoint (Figure 2A). Other factors associated with increased odds of reaching the primary endpoint were age (OR, 1.056; 95% CI, 1.038-1.076; $p < 0.001$), male sex (OR, 1.588; 95% CI, 1.041-2.428; $p = 0.032$), BMI (OR, 1.076; 95% CI, 1.015-1.141; $p = 0.014$), chronic kidney disease (OR, 5.178; 95% CI, 1.151-25.582; $p = 0.038$), and concurrent pneumonia (OR, 4.807; 95% CI, 3.165-7.403; $p < 0.001$) (Figure 2B).

Supplementary Files

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- [Supplementalappendix.docx](#)