Treatment experience of regdanvimab for mild to moderate COVID-19 hospitalized patients in the Delta variant-predominant period in Korea

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Abstract

Background: Regdanvimab is the only monoclonal antibody available in Korea that targets the receptor-binding domain of SARS-CoV-2. Although the efficacy of regdanvimab against the original and beta variant viruses was demonstrated, it remains uncertain whether it has therapeutic effect on delta variant in the real world.

Methods: We retrospectively evaluated the characteristics and clinical outcome of patients hospitalized for COVID-19 and treated with regdanvimab in two university-affiliated hospitals between September and December 2021, during the delta variant-predominant period in Korea.

Results: A total of 374 mild to moderate COVID-19 patients treated with regdanvimab were included in this study. The median age was 65 (interquartile range, IQR 17-92) and 178 (47.6%) patients were male. A total of 322 (86.1%) patients had median 2 (IQR 1-3) risk factors for disease progression. The most common underlying disease was cardiovascular disease (198, 52.9%), followed by diabetes mellitus (95, 25.4%), cancer (40, 10.7%), chronic lung disease (34, 9.1%), immunosuppression (1 7, 4.5%), and chronic kidney disease (12, 3.2%). There were 43 (11.5%) patients with a body mass index ≥ 30. The median time to regdanvimab treatment from symptom onset was 4 (IQR 2-6) days. 226 (60.4%) patients were fully vaccinated, and 109 (29.1%) were not vaccinated at all. 185 (49.5%) patients had pneumonia. Most (342/374, 91.4%) patients improved without any other treatment for COVID-19 and were discharged. Only 32 (8.6%) patients required other therapeutic agents such as remdesivir, corticosteroids or oxygen therapy after regdanvimab administration. The time from regdanvimab infusion to addition of other therapeutic agents was median 5 days (IQR 3-6.5). When comparing the characteristics of 32 patients who needed other treatment with those who improved only with regdanvimab treatment, there was a significant difference in the presence of pneumonia (27/32, 84.4% vs. 158/342, 46.2%, P< 0.001) and there was no significant difference in vaccination status (15/32, 46.9% vs. 211/342 61.7% P=0.101).

Conclusion: This study shows the potential clinical benefits of regdanvimab in mild to moderate COVID-19 patients in the real world during the delta variant predominant period in Korea.

Introduction

- Monoclonal antibodies that target the spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reduce hospitalization, viral titers, and clinical symptoms in patients with coronavirus disease 2019 (COVID-19).
- The effectiveness of different monoclonal antibodies varies dramatically depending on the circulating variant, and the roles played by monoclonal antibodies as treatments for COVID-19 thus remain unclear.
- Regdanvimab (CT-P59, Celltrion, Incheon, Korea) is the only recombinant monoclonal antibody available to treat COVID-19 in Korea. Regdanvimab received conditional approval as an emergency treatment for patients with mild to moderate COVID-19 in February 2021.
- Regdanvimab is effective against the original and Beta variant viruses, but it remains unclear whether it has any therapeutic effect on the Delta variant in real-world situations.

Objective

- we evaluated the clinical characteristics and outcomes of patients hospitalized with COVID-19 who were treated with regdanvimab during Delta variant predominance in Korea.

Methods

- This retrospective study was conducted at two university-affiliated teaching hospitals located in Seoul and Goyang, Korea. In September 2021, the respective hospitals designated 30 and 32 general ward beds for the exclusive care of patients with COVID-19; this was mandated by an Executive Order of the Korean health authority.
- We reviewed the records of all patients with COVID-19 confirmed via real-time reverse transcriptase polymerase chain reaction from September through December 2021. The monthly proportions of the Delta variant in Korea were 96.1 – 100.0% during the study period.
- Of patients hospitalized with COVID-19 during the study period, only those who received regdanvimab were included.
- Regdanvimab was given to patients who did not require oxygen therapy, were within 7 days of symptom onset, and who met at least one of the following criteria: age >50 years, pneumonia evident via chest X-ray or chest computed tomography (CT), or an underlying comorbidity. Underlying comorbidities were diabetes mellitus, obesity (body mass index >30 kg/m^2), immunosuppression, and cardiovascular, chronic respiratory, chronic renal, or chronic liver disease.
- Patients received a single intravenous infusion of 40 mg/kg regdanvimab over 60 - 90 min.
- We excluded patients who required oxygen therapy or other therapeutic agents within 24 h of regdanvimab treatment and in whom the illness progressed rapidly, making it difficult to evaluate the effect of regdanvimab.
- Patients whose medical records were incomplete or who were transferred to tertiary care centers within 24 h of regdanvimab administration were also excluded.
- We collected data on patients' sex and age; dates of symptom onset, admission and discharge; COVID-19 disease severity at admission; underlying diseases; COVID-19 vaccination status; body mass index; regdanvimab administration date; lowest oxygen saturation level on the day of regdanvimab infusion; oxygen therapy or any other treatment during hospitalization; and lung infiltration evident via chest X-ray or CT.
- We also collected data on the fever pattern after regdanvimab administration and adverse reactions associated with regdanvimab. Transfers to other hospitals for intensive care, and deaths during hospitalization were noted.

Results

Table 1. Demographic and clinical characteristics of patients hospitalized with COVID-19 who received regdanvimab from September through December 2021

Characteristics	Number (n = 374)
Age (years)	65 (53 - 75)
Age ≥ 60 years	245 (65.5)
Female	196 (52.4)
Body mass index ≥ 30 kg/m^2	43 (11.5)
Medical comorbidities	299 (79.9)
Cardiovascular disease or hypertension	198 (52.9)
Diabetes mellitus	95 (25.4)
Cancer	40 (10.7)
Chronic lung disease	34 (9.1)
Immunocompromised condition	17 (4.5)
Chronic kidney disease	12 (3.2)
Neurodevelopmental disorder	6 (1.6)
Chronic liver disease	6 (1.6)
Other	37 (17.9)
Number of risk factors	
0	52 (13.9)
1	66 (17.6)
2	126 (33.7)
3	88 (23.5)
4	35 (9.4)
5	7 (1.9)
Severity of disease	
Asymptomatic	26 (7.0)
Mild	172 (46.0)
Moderate	176 (47.0)
Days from symptom onset to admission	3 (2 - 5)
Days from symptom onset to regdanvimab infusion	4 (2 - 6)
Days from admission to regdanvimab infusion	1 (0 - 1)
Duration of hospitalization (days)	8 (6 - 9)
Vaccination status	
Fully vaccinated	226 (60.4)
Partially vaccinated	39 (10.5)
Unvaccinated	109 (29.1)
SpO2 (%) on the day of regdanvimab administration (median, range)	96 (95 - 97)
Radiological evidence of pneumonia (chest X-ray or CT)	185 (49.5)
Chest CT performed	242 (64.7)
Adverse reaction after regdanvimab infusion	15 (4.0)
Rash	5 (1.3)
Itching	5 (1.3)
Nausea/vomiting	3 (0.8)
Fever	2 (0.5)
Diarrhea	1 (0.3)
Use of additional therapeutic agents	32 (8.6)
Oxygen support during admission	15 (4.0)
Dexamethasone and other glucocorticoids	28 (7.5)
Remdesivir	27 (7.2)
Time from regdanvimab Tx to administration of additional therapeutic agents (days)	5 (3 - 7)
Outcome	
Referral to tertiary care center for intensive care	0
In-hospital mortality	0

- Data are nos. (%) or medians (interquartile ranges) unless otherwise indicated.
- Patients were considered fully vaccinated at least 14 days after they received the second dose of ChAdOx1 nCoV-19 (Oxford/AstraZeneca, Cambridge, UK), BNT162b2 (Pfizer/BioNTech, New York, NY, USA and Mainz, Germany), or mRNA-1273 (Moderna, Cambridge, MA, USA); or at least 14 days after receipt of a single dose of Ad26.COV2.S (Janssen, Beerse, Belgium)

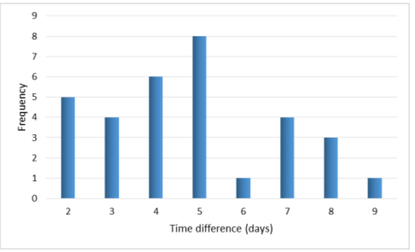

Figure 1. Frequency of time difference (days) between administration of regdanvimab and other therapeutic agents (remdesivir, corticosteroids, oxygen therapy)

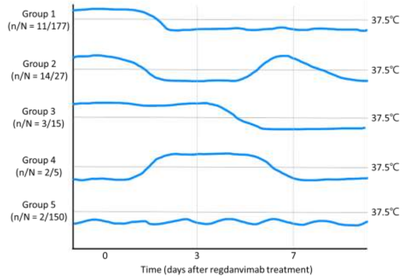

Figure 2. Body temperature patterns of COVID-19 patients treated with regdanvimab

In ***Group 1***, the fever resolved within 3 days after regdanvimab treatment. In ***Group 2***, the fever resolved within 3 days but relapsed. In ***Group 3***, the fever resolved more than 3 days after regdanvimab treatment. In ***Group 4***, no fever was evident on the day of regdanvimab treatment but fever developed later. In ***Group 5***, no fever was apparent during hospitalization.

- n, number of patients who received additional therapeutic agents.
- N, total number in each fever pattern group.

- No study patients died or were transferred to another hospital for intensive care. When the 342 patients treated with regdanvimab only were compared to the 32 patients who received additional therapeutic agents, the pneumonia rate differed significantly (158/342 [46.2%] vs. 27/32 [84.4%], P <0.001).

Conclusions

- Our findings suggest that regdanvimab was therapeutic in patients with mild to moderate COVID-19 during Delta variant predominance. The monoclonal antibody prevented progression to severe disease in most high-risk patients with mild to moderate COVID-19.
- Relapse or persistence of fever after treatment with regdanvimab may not always indicate progression of COVID-19.