Use of Antibody Cocktail, REGN-COV2, in two Non-Hodgkin's Lymphoma (NHL) patients with mild COVID-19 disease, at a tertiary care hospital in South India: A case series

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Abstract

Severe Acute Respiratory Syndrome Corona virus 2 (SARS–CoV-2) is the cause for Corona virus disease 2019 (COVID-19). Most patients have asymptomatic or mild disease. A subset of patients develops moderate, severe or critical disease. The prognosis is dismal with severe and critical disease. REGN-COV2 has been shown to reduce the progression to severe disease in high-risk subjects, by reducing the viral load in the early stages of the illness. We describe two patients with Non-Hodgkin's Lymphoma and COVID 19, who received the antibody cocktail, and did not develop severe disease.

Keywords

SARS–CoV-2, COVID-19, REGN-COV2, CASIRIVIMAB, IMDEVIMAB, Lymphoma

Background

In December 2019, the novel beta corona virus Severe Acute Respiratory Syndrome Coronavirus2 (SARS–CoV-2) emerged as the cause of a respiratory infection known as Corona Virus Disease 2019 (COVID-19) [1]. Although most cases of COVID-19 are asymptomatic or mild, there are a small subset of patients (about 10%) who develop severe disease resulting in hospitalization and death [2]. It was hypothesized that there was immune hypersensitivity to the viral infection, resulting in hypoxemia. This led to multiple studies of various immune modulating agents, with mixed results [3–5]. More recent data have shown high viral titers in hospitalized patients [6].This indicates that patients with mild illness, in whom immune response has not yet initiated, have a therapeutic window, during which time, if viral titres could be reduced or eliminated, can lead to nil or limited host immune response, thus avoiding a cytokine storm.

Cancer and COVID-19

Cancer and COVID-19 are a deadly combination. The pooled incidence of cancer among COVID-19 patients is about 6%. Although all cancers increase the risk of death in COVID-19 patients, patients with lung cancer and hematological malignancies have a slightly higher risk [7,8]. Among patients with COVID-19 and cancer, 39% of patients progressed to severe disease, compared with only 8% of non-cancer COVID-19 patients [9]. Among a cohort of patients with lymphoma and COVID-19, 49% of whom were on active treatment, there was a mortality of 35%. It was also showed that the persistence of SARS-CoV-2-positive polymerase chain reaction after week 6 was significantly associated with mortality [10].

Rationale to use REGN-COV2

REGN-COV2, consisting of CASIRIVIMAB and IMDEVIMAB, is an antibody cocktail made up of two non-competing, neutralizing human IgG1 antibodies that target the receptor binding domain of the SARS-CoV-2 spike protein, thereby preventing viral entry into human cells through the angiotensin-converting enzyme (ACE) [11,12]. It has been shown to reduce viral load, with a greater effect in those patients in whom endogenous immune response had not been initiated, or who had a high viral load at baseline [13]. Combination antibody treatment (cocktail) has been shown to prevent rapid mutational escape, associated with single antibody treatment [11].

Recently,REGN-COV2wasgiven emergency use authorization (EUA) by the FDA for treatment of mild to moderate COVID-19 in adult and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. Among the conditions

mentioned as high risk, immunosuppressive disease or patients currently receiving immunosuppressant drugs are included. This drug is not to be used in patients who have progressed to severe disease and/or are oxygen dependent, where it has shown to worsen outcomes [14].

We present two patients with Non-Hodgkin's Lymphoma and COVID-19, who were on active treatment for their lymphoma, for whom the antibody cocktail REGN-COV2, was used.

Case Presentation

Case 1

A 45-years-old man, presented with dysuria, increased frequency of urination and haematuria for one month. He was evaluated and found to have a bladder mass with obstructive uropathy. He underwent bilateral DJ stenting, bladder biopsy and placement of urinary catheter. Biopsy was reported as high-grade B cell Non-Hodgkin's lymphoma. PET CT showed bladder tumor with extensive disease and bone marrow involvement (stage IV). While being evaluated for his cancer, he was tested for SARS-COV-2 by reverse transcriptase–polymerase chain reaction (RT–PCR), and was found to be positive. His CT severity score was not recorded on the PET CT, done at outside centre, and was assumed to be mild. He was admitted for treatment of his lymphoma. His bloods showed elevated uric acid, deranged electrolytes and high renal parameters. His CRP was elevated. He was started on IV hydration, steroids, heparin and oral chemotherapy with cyclophosphamide. His renal parameters began to improve. In view of high risk of progression to severe illness (COVID pneumonia), he was administered REGN-COV2 on day 5 of illness (600 mg of CASIRIVIMAB and 600 mg of IMDEVIMAB together as IV infusion, with premedication). He was continued on chemotherapy. His renal function recovered completely. On follow up, at two weeks, he did not develop severe COVID-19. He is being continued with IV chemotherapy with rituximab-cyclophosphamide, hydroxydaunorubicin, oncovin and prednisolone (R-CHOP) and is currently on active therapy.

Case 2

A 64-years-old man presented with right inguinal lymph nodal swelling in January 2021. Biopsy was reported as Non- Hodgkin's Lymphoma, Large B cell type. His PET CT showed stage III disease with involvement of inguinal, iliac, para-aortic, bilateral axillary and cervical lymph node chains. He was started on R-CHOP chemotherapy and completed four cycles. Interim PET CT showed almost complete response. He was advised continuation of chemotherapy for 2–4 cycles, maintenance rituximab and radiotherapy to initial bulky sites. He completed one more cycle of chemotherapy. On reviewing for his sixth cycle, he complained of fever and body ache. There was a significant contact history of his daughter being SARS-COV-2 positive by RT–PCR, about 2 weeks prior. He was advised SARS-COV-2 testing, which came back positive. His CT severity score was reported as 0/25. In view of mild disease (all his blood parameters were fairly normal, except for mildly elevated CRP and highly elevated ferritin); he was started on oral aspirin and advised REGN-COV-2 to prevent progression to severe illness (COVID pneumonia). He was administered the same on day 4 of illness. On follow up, at 2 weeks, he did not develop severe COVID-19. He is on active treatment for his lymphoma.

Discussion

Severe COVID-19 is a very difficult disease to treat. The mortality rates range from 30 to 60% [15,16]. Many of these patients also have co-morbidities which increase their risk of mortality. The mortality of patients with COVID-19 and cancer ranges from 12 to 30% in different series from different countries [8,17,18].As discussed above, REGN COV2 can reduce viral load [13], which eliminates the need for an immune response to be mounted by the host, thus reducing the risk of a deranged immune response or cytokine storm, or progression to severe disease, which results in better outcomes.

Conclusion

Patients on active cancer treatment, who test positive for SARS-COV-2, are at high risk for progression to severe illness. REGN-COV-2 is an antibody cocktail which can be used in these patients to reduce the risk of progression to severe illness, thus improving their outcome. REGN-COV-2 should be considered in all cancer patients on active treatment within the first five days of testing positive of SARS-COV-2, prior to the initiation of endogenous immune response.

Competing interest

The authors declare no competing interest.

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