Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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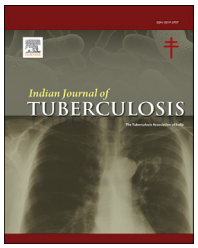

Correspondence

Casirivimab - Imdevimab in Covid 19 – Early Indian experience

Sir,

Corona viruses have traditionally been known to cause disease in humans and animals. By the fag end of the year 2019, medical attention was drawn to an outbreak of pneumonia cases in Wuhan, a city in the Hubei Province of China.[1] A novel corona virus was identified as the culprit which was subsequently designated severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). The disease rapidly spread to vast territories across the globe and has become the worst pandemic of the 21st century. With mounting evidence and clinical experience, if has become clear that most persons who get infected have few or no symptoms despite harboring high viral loads and their condition can be managed on an outpatient basis.[2] Disease progression with development of pneumonia and respiratory failure occurs in a smaller number of persons necessitating hospitalization and administration of supplemental oxygen. Remote (telehealth) management without the need for the patient directly coming into contact with healthcare personnel is an attractive option and is gaining popularity in mild cases.

Risk factors for disease progression and worse outcomes are increasingly being spelt out and subgroup of patients at added risk merit careful monitoring and therapy.[3] It has been postulated that complications and death from Covid-19 are a direct off-shoot of SARS-CoV-2 viral burden and reducing this burden early in the course of disease leads to clinical benefit. Monoclonal antibodies that target spike proteins of SARS-CoV-2 have been evaluated in outpatients with mild to moderate disease and risk factors for severe disease.[4,5] Trial results suggest a benefit from the use of these agents in the form of decreasing need for hospitalisation. In the United States, the monoclonal antibody therapies that have been authorised for emergency in select outpatients at risk for severe disease include Bamlanivimab-etesevimab, Casirivimab-imdevimab and Sotrovimab.[6,7]

Casirivimab – imdevimab is a cocktail made up of two noncompeting, neutralizing human IgG1 antibodies that target the receptor binding domain of the SARS-CoV-2 spike protein and block viral entry into human cells.[8] A "cocktail" approach may prevent the emergence of treatment-resistant mutant virus with usage of a single antibody as has occurred previously when suptavumab, was used to target respiratory syncytial virus. FDA issued an emergency use authorization for the investigational monoclonal antibodies casirivimab and imdevimab for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are ≥12 years of age weighing ≥40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. Regeneron Pharmaceuticals introduced this antibody cocktailunder the name REGEN-COV (casirivimab with imdevimab) and is globally marketed by Roche limited and in India by Cipla pharma under the trade name Ronapreve. Central Drugs Standards Control Organisation (CDSCO) has provided an Emergency Use Authorisation (EUA) for Roche's antibody cocktail (Casirivimab and Imdevimab) in India since May 2021.

The specific challenges regarding the use of this cocktail foreseen in Indian circumstances include

a. The efficacy of the agent against variants of the SARS-CoV-2 that are prevalent in the country,
b. The economic burden of procuring the drug in our patients, considering the fact that most of our patients do not have third party assistance and pay out of pocket for health care related expenses
c. The potential difficulties of administering the agent in an outpatient setting observing full infection control precautions.[9]

The cocktail is available as a vial which has adequate dose for administration to two individuals. Once opened and reconstituted, it should be administered within 48 hours after storage at 4–8C. So, the clinician has the added task of identifying a second patient with indications who can share the vial.

We share the clinical data and results of our first 29 patients in whom the agent was administered. The drug was offered to 146 patients of whom 29 decided to go ahead with administration of the agent. Reasons for opting out included

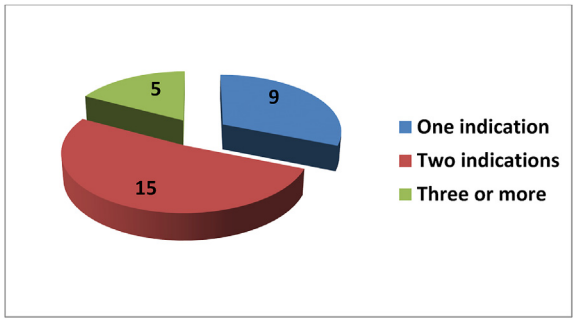

Fig. 1 – Number of high risk factors for administering casirivimab imdevimab in individual Covid 19 outpatients.

cost of therapy and lack of concern towards disease progression. The patients included out patients and covid patients admitted for reasons other than covid. The drug was administered in the Covid 19 in-patient ward (for out-patients also) and they were observed for a period of four hours for any adverse reactions. Of the patients in whom the drug was used, more than 50% had two indications. Fig. 1 depicts the number of indications that the patients had. Diabetes mellitus, chronic kidney disease, age >65 years, COPD etc were the common risk factors which necessitated antibody cocktail treatment. Table 1 summarises the indications in those patients who were given the antibody cocktail.

The agent was well tolerated in all patients in whom it was administered. No anaphylaxis was reported and no treatment related adverse event was noted. One patient with coronary artery disease, who was admitted with left ventricular failure turned out to be Covid 19 antigen positive at admission and received the drug. He expired after 48 hours with worsening pulmonary edema. Two patients had worsening of covid disease and hypoxia necessitating admission. The drug had good results in 26 patients who did not have worsening of covid disease, emergency visits or hospitalisation. 24 out of this 26 patients reported significant relief of their symptoms (fever, myalgia or fatigue) within 48 hours of drug administration. Fig. 2 summarises the results of therapy with casirivimab imdevimab in our patients, Overall, our preliminary experience suggests that casirivimab imdevimab monoclonal antibody cocktail for covid 19 is safe and efficacious in Indian patients. Larger experience in terms of patient numbers and participating centres is expected to throw more clarity in this subject.

Table 1 – Common indications for administering monoclonal antibody cocktail in covid 19 outpatients.

Indications	Number of patients	Percentage
Diabetes mellitus	14	48.27
Chronic kidney disease	17	58.62
Age >65 years	12	41.37
COPD	11	37.93
Immunosuppressive treatment	5	17.24
Obesity	4	13.79
Cardiovascular disease	5	17.24

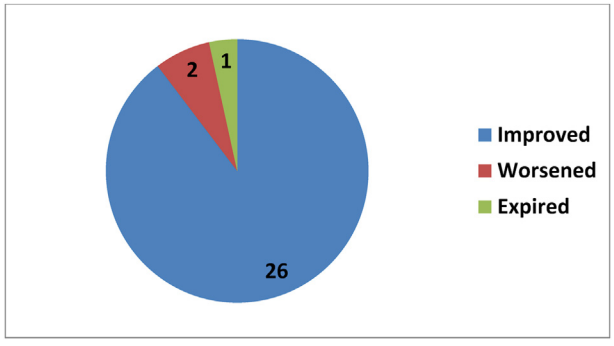

Fig. 2 – Results of therapy with casirivimab imdevimab in Covid 19 outpatients.

Conflicts of interest

The authors have none to declare.

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Rajesh Venkitakrishnan*
Jolsana Augustine
Divya Ramachandran
Melcy Cleetus
Rajagiri Hospital, Kochi, India

*Corresponding author. Tel.: +91-9745501976.
E-mail address: rajeshdhanya@rediffmail.com
(R. Venkitakrishnan)

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