COVID-19 vaccination and immunomodulatory or immunosuppressive drugs: indications and contraindications

To the Editor,

The COVID-19 pandemic has taken millions of human lives and is still accelerating to severely affect globally. With the advent of SARS-CoV-2 vaccines viz, mRNA, recombinant adenovirus vector and whole virion inactivated vero cell, which are inactivated vaccines having emergency use authorisation granted by the US Food and Drug Administration on 11 December 2020, led to a ray of hope in the COVID-19 pandemic. Immunotherapy has shown an importance in treating severe COVID-19, but the development of vaccine has been considered to be crucial for protecting the uninfected. The Australasian medical dermatology group strongly recommended COVID-19 vaccination in patients on immunomodulatory or biological agents as no specific contraindication or identifiable safety issues have been identified until.[1] According to public health England's immunisation against infectious disease, patients on immunosuppressed medications are extremely vulnerable and should be vaccinated.[2] Patients who are on long-term immunosuppressive medications, such as methotrexate, cyclophosphamide, mycophenolate, systemic corticosteroids for more than a month and biological therapies such as anti-TNF (Tumour necrosis factor) and anti-CD20 monoclonal antibodies, may be considered as priority for vaccination.

Systemic corticosteroids affect vaccine efficacy in a dose-dependent manner. In a longitudinal study, it was found that >10 mg/day was associated with impaired humoral immunity.[3]

Rituximab and methotrexate have also been shown to reduce humoral response to seasonal influenza and pneumococcal vaccines. Drug-induced B cell inhibition would not influence innate and CD8 T cell responses, which are central to SARS-CoV-2 elimination. The British Society of Rheumatology advised COVID-19 vaccine course should be given 4 weeks or more prior to rituximab; moreover, suboptimal response is expected within 6 months of last rituximab infusion. Patients with rheumatoid arthritis, when vaccinated with influenza, hepatitis vaccines showed markedly blunting of seroconversion for 6–10 months after rituximab infusion.[4] However, early data from case reports have suggested poor outcomes in patients with rituximab-treated COVID-19. Such data are a red alert and reinforce the necessity of its judicious use for the most clinically crucial cases during this pandemic.

Methotrexate cause humoral suppression by interaction with the B cell activation factor and increasing immunosuppressive adenosine and regulatory B cells. It has been seen that immunogenicity of influenza vaccine significantly improved by temporarily discontinuing methotrexate for 2 weeks post-vaccination without causing an increase in rheumatoid arthritis disease activity. According to Public Health England's immunisation against infectious disease, patients who are planned for immunosuppressive therapy, either methotrexate or cyclophosphamide, should ideally be vaccinated 2 weeks prior to their commencement.[2]

Azathioprine and mycophenolate mofetil have both shown to decrease the antibody titres after vaccination but not below the threshold seroprotection level; therefore, it is recommended to continue the treatment.

Anti-TNF agents have shown safety in context of live varicella-zoster vaccine.[5] It has been advised to continue these agents in vaccination drive as they also have been associated with a decrease in severity and hospitalisation of patients with COVID-19.

Tofacitinib also have been shown to be safe in context with varicella-zoster vaccine. Discontinuation for 1 week before and after vaccination, yielded no effect in patients reaching serprotection.

Available COVID-19 vaccines are not contraindicated in patients on immunomodulatory or immunosuppressive agents, although it is indicated in most of the available

Table 1 Indications for COVID-19 vaccination in patients on immunomodulatory or immunosuppressive agents

S No	Drugs	Recommendations	Vaccination indicated or contraindicated
1.	Systemic corticosteroids	Prednisolone equivalent <10 mg/day	Indicated
2.	Methotrexate	Temporary cessation of methotrexate for 2 weeks post-vaccination	Indicated
3.	Azathioprine, mycophenolate mofetil, hydroxychloroquine, leflunomide and sulfasalazine	Continuation of the drugs during vaccination	Indicated
4.	Anti-TNF (Tumour necrosis factor) agents	Continuation during vaccination	Indicated
5.	Anti-CD20	4 weeks prior and 6 months after vaccination	Indicated
6.	JAK (Janus kinase) inhibitors	Discontinuation 1 week before and after vaccine	Indicated

JAK, Janus kinase; TNF, Tumour necrosis factor.

data (table 1). With time, further experiences and knowledge would emerge that may help and guide treatment selection within the existing and post-COVID-19 era.

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