Toward a COVID-19 vaccine strategy for patients with pemphigus on rituximab

To the Editor: Shakshouk et al and Schultz et al discuss the potential impact of rituximab-induced peripheral B-cell depletion on future COVID-19 vaccine response. Their articles highlight the need for emergent study of anti-CD20 therapy's impact on COVID-19 vaccine response. Here, we review existing data surrounding the vaccination of individuals receiving anti-CD20 monoclonal antibodies.

The effect of rituximab and other anti-CD20 monoclonal antibodies on vaccine response has been studied for inactivated vaccines, including those for seasonal influenza, hepatitis B, tetanus, shingles, pneumococcus, and *Haemophilus influenzae* type b.[1,2] These studies suggest that rituximab recipients mount attenuated yet meaningful vaccine responses.[1] Additionally, these studies indicate that rituximab recipients are not at increased risk of inactivated vaccine-related adverse effects.[3] Recently, a prospective clinical trial evaluated the effect of ocrelizumab (humanized anti-CD20 antibody) on the immunogenicity of several vaccines that were administered 12 weeks after infusion.[4] This study showed increased seroprotection rates across all studied vaccines in ocrelizumab recipients, although these conversion rates are lower than those observed in control individuals. Consensus guidelines recommend administering routine vaccinations (eg, tetanus, diphtheria, and pertussis [TDaP]) at least 4 weeks before rituximab initiation.[3] Notably, they recommend administering inactivated influenza vaccine even in individuals undergoing active treatment with rituximab, because patients face imminent risk of contracting influenza, which outweighs the minimal risks associated with vaccination.[3]

Importantly, there are no studies addressing the immunogenicity of live attenuated vaccines, given theoretical safety concerns regarding the use of live attenuated vaccines in rituximab recipients.[3] Additionally, there are no studies that have evaluated the safety and immunogenicity of messenger RNA vaccines or viral vector vaccines, which are among the leading COVID-19 vaccine candidates, because no vaccines in these classes are commercially available.

How should dermatologists approach vaccination of rituximab recipients with a future COVID-19 vaccine? Although the answer will depend on the type(s) of vaccine(s) that reach the market, inoculation with vaccines that do not contain live virus particles (eg, inactivated vaccines, messenger RNA vaccines) should be considered in the absence of postmarketing data or vaccine trial signals suggesting previously unforeseen risk.[5] We assess that COVID-19 vaccine recommendations similar to influenza vaccine recommendations are sensible until COVID-19 vaccine response data for individuals receiving rituximab emerges.

The ideal timing of vaccination is unknown; however, individuals who have not initiated rituximab therapy are typically vaccinated at least 4 weeks before rituximab infusion. Individuals who are actively receiving rituximab are often vaccinated against influenza 12 to 20 weeks after completion of a treatment cycle so that patients have 4 weeks or longer before their next infusion (assuming dosing every 6 months) to mount an immune response.[3] Extending rituximab dosing intervals to enhance vaccine response should be weighed against the risk of disease recurrence. Although vaccine response may be attenuated and may occur at lower rates in rituximab recipients, vaccine response can be quantified with titers, which may be helpful for guiding decisions to revaccinate patients after humoral immune reconstitution (approximately 6-9 months after rituximab discontinuation).

Until COVID-19 vaccines arrive, the data encourage careful use of anti-CD20 therapy for skin disease. When vaccines are available, dermatologists can consider vaccinating patients 12 to 20 weeks after the completion of a treatment cycle or extending rituximab dosing intervals.

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REFERENCES

1. Baker D, Roberts CAK, Pryce G, et al. COVID-19 vaccine-readiness for anti-CD20-depleting therapy in autoimmune diseases. *Clin Exp Immunol*. 2020;202(2):149-161.
2. Houot R, Levy R, Cartron G, Armand P. Could anti-CD20 therapy jeopardise the efficacy of a SARS-CoV-2 vaccine? *Eur J Cancer*. 2020;136:4-6.
3. Mohme S, Schmalzing M, Müller CSL, Vogt T, Goebeler M, Stoevesandt J. Immunizations in immunocompromised patients: a guide for dermatologists. *J Dtsch Dermatol Ges*. 2020;18(7):699-723.
4. Bar-Or A, Calkwood JC, Chognot C, et al. Effect of ocrelizumab on vaccine responses in patients with multiple sclerosis: the VELOCE study. *Neurology*. 2020;95(14):e1999-e2008.
5. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines—a new era in vaccinology. *Nat Rev Drug Discov*. 2018;17(4):261-279.

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