The Utilization of B Cell Therapy in Conjunction with RNA-Based COVID-19 Vaccines

Naveen Malik, Robert Cain* and Michal Sly
Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Corresponding Author*
Robert Cain
Department of Neurology
Massachusetts General Hospital
Harvard Medical School
Boston, USA
Cainrb121@mgh.havard.edu

Received date: 17-August-2023, **Manuscript No:** JMSO-23-113650; **Editor assigned:** 19-August-2023, PreQC No. JMSO-23-113650(PQ); **Reviewed**: 27-August-2023, QC No. JMSO-23-113650(Q); **Revised date**: 28-August-2023, Manuscript No: JMSO-23-113650(R); **Published date:** 30-August-2023, DOI: 10.35248/2376-0389.23.10.8.511

Introduction

As an increasing number of individuals gain access to COVID-19 vaccines, there is growing concern among those with conditions like Multiple Sclerosis (MS), Neuromyelitis Optica (NMO), and individuals taking immunosuppressive medications regarding the safety and effectiveness of these vaccines. Of particular interest are drugs like Rituximab, Ocrelizumab, and the recently approved of Atumamab, which deplete B cells by targeting the CD20 receptor. Previous studies have hinted at reduced vaccine-induced protection when CD20 is blocked [1,2]. Although no published data currently exists on COVID-19 vaccine efficacy in immunosuppressed populations, there is a lively debate about whether CD20-blocking immunotherapy could impact the effectiveness of the new RNA-based COVID-19 vaccines.

The protection provided by vaccines relies on two primary mechanisms: humoral immunity (mainly mediated by antibodies and B cells) and cellular immunity (mainly driven by T cells) [3]. The sustained cellular immunity, which defends against intracellular pathogens like viruses, depends on CD8+ T cells, which become activated in response to foreign antigens presented by infected cells. On the other hand, humoral immunity primarily guards against extracellular pathogens. These pathogens interact with circulating antibodies or B cells through antigen-specific B cell receptors [4]. The CD20 receptor is expressed on the surface of developing B lymphocytes. Therefore, therapeutic monoclonal antibodies targeting CD20 deplete these circulating B cells and specifically disrupt the development of new memory B cells and antibody-producing plasma cells responsible for humoral immunity [5,6].

Previous research on vaccine responses in patients receiving anti-CD20 therapies has primarily focused on rituximab and Ocrelizumab. In a prospective controlled study involving rituximab-treated patients with rheumatoid arthritis, it was observed that predominantly B cell-dependent vaccine responses (to vaccines like pneumococcal vaccine and the Neoantigen, Keyhole Limpet Hemocyanin (KLH)) were reduced, while responses more reliant on T cells (measured through the reaction to tetanus toxoid vaccine and the delayed-type hypersensitivity response) remained intact in both groups [7]. Additionally, the 'Study to Evaluate the Effects of Ocrelizumab on Immune Responses in Participants With Relapsing Forms of Multiple Sclerosis' (VELOCE) was conducted to specifically assess humoral responses to various non-COVID-19 inactivated vaccines in Ocrelizumab-treated multiple sclerosis patients [1]. This study demonstrated weakened humoral responses, as measured by antibody titers, to vaccines containing tetanus toxoid, Pneumovax, KLH, and influenza in Ocrelizumab-treated patients. However, it's worth noting that cellular immunity responses to the vaccines were not investigated [1]. The trial primarily focused on antibody titers, and it is known that anti-CD20 medications disrupt the formation of new memory B cells and reduce antibody production. Nevertheless, vaccine effectiveness is not solely reliant on antibodies, and no study has directly examined infection rates following vaccination, primarily because baseline rates of most vaccine-preventable diseases are extremely low. Consequently, the critical question of whether patients taking CD20-depleting medications receive less real-world protection from vaccines remains unanswered.

However, how does this previous data relate to the new mRNA-based vaccines? Both the approved Moderna vaccine and the BioNTech/Pfizer vaccine are Lipid-Nanoparticle Formulated (LNP), nucleoside-modified RNA vaccines encoding the SARS-COV-2 spike (S) glycoprotein. Thus far, there is no in-vivo data about the efficacy of these vaccines in immunosuppressed patients or those undergoing B cell depleting therapy. A case report was recently published involving a patient treated with Ocrelizumab who received the Pfizer mRNA COVID-19 vaccine and failed to develop detectable antibodies 27 days after the second vaccine dose [8,9]. However, it's important to note that the absence of antibody production does not necessarily equate to lack of vaccine efficacy. Preliminary studies suggest that mRNA vaccines engage both humoral and cellular immunity mechanisms. A phase I/II study of an mRNA vaccine candidate, BNT162b1, which is closely related to the Moderna COVID vaccine, showed a robust cellular immune response, including a skewed T-helper type 1 (Th1) response, interferon-γ production by CD8+ and CD4+ T cells, and expansion of memory T cells. While B cells typically play a role in T cell activation, they may not be essential for generating a response. Consequently, one could speculate that mRNA vaccines might remain effective in individuals using B cell depleting drugs due to the preservation of the T cell response.

While B cell depleting drugs effectively remove 95%-100% of B cells from the bloodstream and likely also affect the bone marrow and lymph nodes, complete depletion of B cells in other tissues is less likely[9,10]. Different B cell depleting drugs have varying levels of penetration into tissues, and B cells from various compartments may be recruited to sites of inflammation [11].Therefore, individuals treated with rituximab who receive a COVID vaccine may still experience a partial humoral response.

To better understand the balance between humoral and cellular immunity in generating a protective response to SARS-COV-2 vaccines in individuals receiving anti-CD20 therapy, further prospective clinical studies will be necessary. It is reasonable to speculate that mRNA vaccines may induce reduced humoral responses in this population compared to the general population, but the actual impact on vaccine effectiveness remains uncertain. Both patients and healthcare providers are grappling with questions about whether to delay or adjust anti-CD20 therapy, synchronize vaccination with the end of the anti-CD20 therapy cycle, or aim for early vaccination without changes to immunosuppressive treatment.

Given the ongoing significant risk posed by COVID-19 and the assumption that the vaccine will be safe and at least partially effective in patients on anti-CD20 therapy, we argue against systematically postponing vaccination or delaying anti-CD20 therapy. When considering whether to defer or adjust immunosuppressive therapy, the decision should be individualized based on the assessed risk of delaying anti-CD20 treatment. Patients with less severe or low-risk neurological conditions may reasonably choose to delay therapy due to theoretical concerns about vaccine efficacy. In contrast, those for whom delaying anti-CD20 therapy poses a higher risk may continue without modifications.

Additionally, there isn't strong evidence to support switching from anti-CD20 therapy to alternative disease-modifying treatments, as there is a potential risk that other therapies targeting T cells or having nonspecific

affects might also impact vaccine efficacy by reducing cellular immune responses. Questions also remain about the potential need for booster doses of the vaccines in this population, and if needed, determining the timing and dosage of these boosters.

The persistent high prevalence of COVID-19 provides a unique opportunity to investigate infection rates following mRNA vaccination in individuals using B cell depleting drugs. While previous studies of vaccination efficacy have mainly relied on biomarkers of immunogenicity, particularly humoral immunity, to predict protection against infection, the ongoing pandemic allows for a direct examination of the impact of anti-CD20 therapy on vaccine efficacy by measuring infection rates. Currently, there are more questions than answers regarding COVID-19 vaccines in immunosuppressed patients, but making decisions about deferring or altering anti-CD20 therapy to optimize COVID-19 vaccine effectiveness remains a complex challenge.

References

1. Bar-Or, Amit, et al. "Effect of ocrelizumab on vaccine responses in patients with multiple sclerosis: the VELOCE study." *Neurology* 95.14 (2020): e1999-e2008.
2. Bingham III, Clifton O., et al. "Immunization responses in rheumatoid arthritis patients treated with rituximab: results from a controlled clinical trial." *Arthritis Rheum. Off. J. Am. Coll. Rheumatol.* 62.1(2010): 64-74.
3. Clem, Angela S. "Fundamentals of vaccine immunology." *J. glob. infect. dis.* 3.1(2011): 73.
4. Ineichen, Benjamin V., et al. "Rituximab treatment for multiple sclerosis." *Mult. Scler. J.* 26.2(2020): 137-152.
5. Hughes, Richard, et al. "COVID-19 in ocrelizumab-treated people with multiple sclerosis." *Mult. scler. relat. disord.* 49(2021).
6. Hauser, Stephen L., et al. "Ofatumumab versus teriflunomide in multiple sclerosis." *N. Engl. J. Med.* 383.6(2020): 546-557.
7. MOC, C. "The effect of disease-modifying antirheumatic drugs on vaccine immunogenicity in adults." Cleve Clin J Med 87.11(2020): 695.
8. Killestein, Joep, Renaud Du Pasquier, and Bernhard Hemmer. "Vaccination in B-cell–depleted patients with multiple sclerosis." *Neurology* 95.14(2020): 613-614.
9. Kunkel, Eric J., and Eugene C. Butcher. "Plasma-cell homing." *Nat. Rev. Immunol.* 3.10(2003): 822-829.
10. Myhr, Kjell-Morten, et al. "B cell depletion in the treatment of multiple sclerosis." *Expert opin. biol. ther.* 19.3(2019): 261-271.
11. Thurlings, Rogier M., et al. "Synovial tissue response to rituximab: mechanism of action and identification of biomarkers of response." *Ann. rheum. dis.* 67.7(2008): 917-925.

Cite this article: Malik N., et al. The Utilization of B Cell Therapy in Conjunction with RNA-Based COVID-19 Vaccines. j mult scler 2023,10(8), 511