



## Letter to the Editor

**Multiple sclerosis, B cell therapy, and the COVID-19 vaccine**

Dear editor

The first COVID-19 vaccine has been approved in the United States by the FDA for emergency use [5,6]. Healthcare workers will have the earliest access, so individual providers must decide quickly on receiving the vaccine. While it appears safe in healthy individuals, this decision is more complicated for healthcare providers with autoimmune diseases. This is especially true for providers with multiple sclerosis on B cell depleting therapies.

B cell depleting therapies, such as ocrelizumab and rituximab, diminish the immunization effect of vaccines, although the degree of effect varies by vaccine and timing [1–3]. Recommendations are to vaccinate prior to starting B cell depleting therapy [4]. Previously formed immune responses are not diminished by treating with B cell depleting therapy after immunization [1]. If already on B cell depleting therapy, treating later seems to be more effective. Waiting 6 months post-infusion to get vaccinated is more effective than 2 months post-infusion based on studies with rituximab [3]. While these early studies with rituximab in rheumatological disorders suggested that vaccination 1–2 months after rituximab infusion created very minimal response, the futility of early post-infusion vaccination has been challenged by more recent studies. In the VELOCE study in patients with relapsing remitting multiple sclerosis, significant although reduced responses to multiple vaccines were observed when given 3 months after ocrelizumab [1]. CD19 levels are effectively depleted within 2 weeks of ocrelizumab infusion and remain depleted up to 6 months or longer in the majority of patients [1]. It seems unlikely that vaccination 1–2 months earlier would be ineffective when compared to the modest effectiveness of 3 month post-infusion vaccination, especially considering that B cells were similarly depleted. In fact, a more systemic B cell depletion is believed to occur by 3 months post-infusion [1]. Overall, vaccination before ocrelizumab is the most effective method, but this is not always feasible. In patients on ocrelizumab, treating at end of an infusion cycle is likely better than treating early in the cycle. If able to maintain disease control, delaying the subsequent infusion may allow for a better vaccine response. In all other patients in the midst of an infusion cycle, some vaccination response is better than none.

The vaccine timing issue in regards to B cell depletion therapy is further complicated for COVID-19 vaccines. As vaccine availability will be initially sparse, selective timing of vaccination is an unlikely luxury for healthcare workers on B cell depletion therapy. Delaying or declining a vaccine opportunity could delay access to a vaccine by many months. Again, some COVID-19 vaccine protection is better than none.

The potential for severe COVID-19 infection is higher in patients with multiple sclerosis who are older, have cardiovascular or pulmonary comorbidities, and have significant baseline disability, and B cell depleting therapies may increase the risk as well [7]. For such high risk patients, it is prudent to consider B cell depleting therapy

discontinuation [8]. Healthcare workers are at high risk of infection given occupational exposures. While initial safety reports from the COVID-19 vaccine trials are promising [5], the potential adverse effects to patients with multiple sclerosis on disease modifying therapies are not known. Some patients with autoimmune diseases were included in the phase 2/3 trials of Pfizer-BioNTech COVID-19 vaccine although safety monitoring is still ongoing [6]. Safety in immunocompromised patients is not yet defined. Expectedly, the potential risk to immunocompromised patients is low as these are not live vaccines, and patients who are immunocompromised are not contraindicated from receiving the vaccine [5]. At this time, the benefits of preventing a COVID-19 infection outweighs the possible risks of vaccination.

This dilemma is not only a professional concern, but a personal one. I am a clinically practicing neurologist with multiple sclerosis who is taking B cell depleting therapy. COVID-19 infection and hospitalization rates are rising throughout the United States and is unlikely to improve anytime soon. Risk of infection for healthcare workers like myself continues to rise as well, and infected providers can spread the virus to their patients. Vaccination is our best chance of protecting ourselves and our patients from this terrible disease. I will be taking the first available COVID-19 vaccine, and I am recommending it for my patients in healthcare.

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**References**

- [1] Amit Bar-Or, Jonathan C. Calkwood, Cathy Chognot, Joanna Evershed, Edward J. Fox, Ann Herman, Marianna Manfrini, John McNamara, Derrick S. Robertson, Daniela Stokmaier, Jeanette K. Wendt, Kevin L. Winthrop, Anthony Traboulsee, Effect of ocrelizumab on vaccine responses in patients with multiple sclerosis the VELOCE study, *Neurology* 95 (14) (Oct 2020) e1999–e2008, <https://doi.org/10.1212/WNL.00000000000010380>.
- [2] Christien Rondaan, et al., Efficacy, immunogenicity and safety of vaccination in adult patients with autoimmune inflammatory rheumatic diseases: a systematic literature review for the 2019 update of EULAR recommendations, *RMD Open* 5 (2) (9 Sep. 2019), e001035, <https://doi.org/10.1136/rmdopen-2019-001035>.
- [3] S. van Assen, A. Holvast, C.A. Benne, M.D. Posthumus, M.A. van Leeuwen, A. E. Voskuyl, M. Blom, A.P. Risselada, A. de Haan, J. Westra, C.G. Kallenberg, M. Bijl, Humoral responses after influenza vaccination are severely reduced in patients with rheumatoid arthritis treated with rituximab, *Arthritis Rheum.* 62 (1) (2010 Jan) 75–81, <https://doi.org/10.1002/art.25033>, 20039396.
- [4] Genentech, Ocrevus: Highlights of Prescribing Information, 2019. Available at: [gene.com/download/pdf/ocrevus\\_prescribing.pdf](http://gene.com/download/pdf/ocrevus_prescribing.pdf). Accessed December 2019.
- [5] Fact Sheet For Healthcare Providers Administering Vaccine (Vaccination Providers), Emergency Use Authorization (Eua) Of The Pfizer-Biontech Covid-19 Vaccine To Prevent Coronavirus Disease 2019 (COVID-19), Pfizer-BioNTech COVID-19 Vaccine EUA Fact Sheet for Healthcare Providers, December, 2020. [fda.gov](http://fda.gov).
- [6] Emergency Use Authorization (EUA) for an Unapproved Product Review Memorandum: Pfizer-BioNTech COVID-19 Vaccine Emergency Use Authorization Review

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Memorandum. \*Emergency Use Authorization for Pfizer-BioNTech COVID-19 Review Memo. [fda.gov](https://www.fda.gov), 2020.

- [7] C. Louapre, N. Collongues, B. Stankoff, C. Giannesini, C. Papeix, C. Bensa, R. Deschamps, A. Créange, A. Wahab, J. Pelletier, et al., Clinical characteristics and outcomes in patients with Coronavirus Disease 2019 and multiple sclerosis, *JAMA Neurol.* 77 (9) (2020 Sep 1) 1079–1088, <https://doi.org/10.1001/jama-neurol.2020.2581>. PMID: 32589189; PMCID: PMC7320356.
- [8] W. Brownlee, D. Bourdette, S. Broadley, J. Killestein, O. Ciccarelli, Treating multiple sclerosis and neuromyelitis optica spectrum disorder during the COVID-19 pandemic, *Neurology* 94 (22) (Jun 2020) 949–952, <https://doi.org/10.1212/WNL.0000000000000950>.