



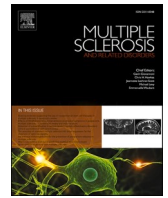
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Importance of T-cell response to COVID-19 vaccination in patients with multiple sclerosis treated by anti-CD20 therapies: New vaccines are required to be developed

I eagerly read Iannetta et al.'s article on T-cell response to SARS-CoV-2 in patients with multiple sclerosis (MS) treated by Ocrelizumab (Iannetta et al., 2021). This article indicated that despite sharp decrease in B lymphocyte counts in these patients, CD4 + and CD8 + T-cell absolute and relative counts were normal in all five patients. This finding could explain the conflicting evidence on the effect of these kinds of drugs (anti-CD 20 therapies) on the incidence or mortality of MS patients who are infected by COVID-19. Although a number of studies have reported an increase in COVID-induced deaths in MS patients treated with rituximab (Calderón-Parra et al., 2021), other studies have reported only an increase in the incidence (Sahraian et al., 2020) and in some others, a lack of the effect of these drugs on the incidence, hospitalization, or death of patients with COVID-19 were reported (Montero-Escribano et al., 2020). Iannetta et al.'s article can describe this contradiction. In fact, it is true that antibodies in these patients may not be produced or are produced in small quantities, but the appropriate response of T cells can be a reason for the good prognosis of COVID-19 in a high percentage of patients consuming these drugs. There is a similar concern about the immune response in these patients to COVID-19 vaccine. Some studies were published on reducing vaccination response in these patients (Louapre et al., 2021). However, the important point in these studies is that most of them have examined the amount of antibodies produced in these patients after vaccination. To my knowledge, only one study has examined the response of T cells after vaccination in the patients receiving immunosuppressive drugs, which showed that despite the reduced humoral response, T-cell response was appropriate in these patients (Prendecki et al., 2021).

There has not been any study on the development of COVID-19 in patients taking these drugs after vaccination; however, it seems that due to appropriate T-cell response, despite the reduced humoral response, the incidence of COVID-19 development in MS patients should be significantly reduced after the vaccination. Hence, this claim requires further studies.

The next issue is the future development of anti-COVID vaccines based on above findings. We know that these vaccines stimulate humoral and cellular immune systems (Ewer et al., 2021). Moreover, studies showed that cellular response occurs much faster (Kalimuddin et al., 2021). Furthermore, as it is observed, the cellular response is of greater importance in the recipients of above drugs. Therefore, it may be necessary to develop vaccines that further stimulate the cellular response of immune system, thereby helping prevent COVID-19 in the patients receiving anti-CD 20 therapies.

Conflict of Interest

The author declares there is no conflict of interest.

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References

- Iannetta, M, Landi, D, Cola, G, Malagnino, V, Teti, E, Fraboni, D, Buccisano, F, Grelli, S, Coppola, L, Campogiani, L, Andreoni, M, Marfia, GA, Sarmati, L., 2021. T-cell responses to SARS-CoV-2 in multiple sclerosis patients treated with ocrelizumab healed from COVID-19 with absent or low anti-spike antibody titers. *Mult. Scler. Relat. Disord.* 55, 103157.
- Calderón-Parra, J, Múñez-Rubio, E, Fernández-Cruz, A, García, Sánchez MC, Maderuelo-González, E, López-Dosil, M, Calvo-Salvador, M, Baños-Pérez, I, Valle-Falcones, M, Ramos-Martínez, A, 2021. Incidence, clinical presentation, relapses and outcome of SARS-CoV-2 infection in patients treated with anti-CD20 monoclonal antibodies. *Clin. Infect. Dis.* ciab700.
- Sahraian, MA, Azimi, A, Navardi, S, Ala, S, Naser, Moghadasi A, 2020. Evaluation of the rate of COVID-19 infection, hospitalization and death among Iranian patients with multiple sclerosis. *Mult. Scler. Relat. Disord.* 46, 102472.
- Montero-Escribano, P, Matías-Guiu, J, Gómez-Iglesias, P, Porta-Etessam, J, Pytel, V, Matias-Guiu, JA., 2020. Anti-CD20 and COVID-19 in multiple sclerosis and related disorders: a case series of 60 patients from Madrid, Spain. *Mult. Scler. Relat. Disord.* 42, 102185.
- Louapre, C, Ibrahim, M, Maillart, E, Abdi, B, Papeix, C, Stankoff, B, Dubessy, AL, Bensa-Koscher, C, Créange, A, Chamekh, Z, Lubetzki, C, Marcelin, AG, Corvol, JC, Pourcher, V, 2021. COVISEP and Bio-coco-neuroscience study group. Anti-CD20 therapies decrease humoral immune response to SARS-CoV-2 in patients with multiple sclerosis or neuromyelitis optica spectrum disorders. *J. Neurol. Neurosurg. Psychiatry.* jnnp-2021-326904.
- Prendecki, M, Clarke, C, Edwards, H, McIntyre, S, Mortimer, P, Gleeson, S, Martin, P, Thomson, T, Randell, P, Shah, A, Singanayagam, A, Lightstone, L, Cox, A, Kelleher, P, Willicombe, M, McAdoo, SP., 2021. Humoral and T-cell responses to SARS-CoV-2 vaccination in patients receiving immunosuppression. *Ann. Rheum. Dis.* annrheumdis-2021-220626.
- Ewer, KJ, Barrett, JR, Belij-Rammerstorfer, S, Sharpe, H, Makinson, R, Morter, R, Flaxman, A, Wright, D, Bellamy, D, Bittaye, M, Dold, C, Provine, NM, Aboagye, J, Fowler, J, Silk, SE, Alderson, J, Aley, PK, Angus, B, Berrie, E, Bibi, S, Cicconi, P, Clutterbuck, EA, Chelysheva, I, Folegatti, PM, Fuskova, M, Green, CM, Jenkin, D, Kerridge, S, Lawrie, A, Minassian, AM, Moore, M, Mujadidi, Y, Plested, E, Poulton, I, Ramasamy, MN, Robinson, H, Song, R, Snape, MD, Tarrant, R, Voysey, M, Watson, MEE, Douglas, AD, Hill, AVS, Gilbert, SC, Pollard, AJ, Lambe, T, 2021. Oxford COVID Vaccine Trial Group. T cell and antibody responses induced by a single dose of ChAdOx1 nCoV-19 (AZD1222) vaccine in a phase 1/2 clinical trial. *Nat. Med.* 27 (2), 270–278.
- Kalimuddin, S, Tham, CYL, Qui, M, de Alwis, R, Sim, JXY, Lim, JME, Tan, HC, Syenina, A, Zhang, SL, Le Bert, N, Tan, AT, Leong, YS, Yee, JX, Ong, EZ, Ooi, EE, Bertolotti, A, Low, JG, 2021. Early T cell and binding antibody responses are associated with COVID-19 RNA vaccine efficacy onset. *Med (N Y).* 2 (6), 682–688.e4.

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