Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Multiple Sclerosis and Related Disorders 64 (2022) 103938

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard

Correspondence

Temelimab for MS and SARS-CoV-2: Could it be a double-edged blessing?

Human Endogenous Retroviruses (HERVs) are genetic remnants embedded in the human genome (~8%), as a result of ancient retroviral infections, amongst which the HERV-W subgroup has been thoroughly investigated. If HERVs aren't expressed in thymus during immunological tolerance development, they could be mistaken as neoantigens, and, additionally, they share sequence homologies with their forebears after deriving from foreign viruses, that could result in antigenic epitopes being recognized by lymphocytes (molecular mimicry). HERV-W hyperexpression has been revealed in a wide range of pathological conditions including placental, autoimmune, neurological and neuropsychiatric pathologies; yet, the observed expression profiles were not connected to any specific HERV-W sequence, prohibiting a definite correlation (Grandi and Tramontano, 2017). Dysimmunity and inflammation in Multiple Sclerosis (MS) have also been linked with HERV-W.

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was identified from a cluster of pneumonia cases in Wuhan, China, and resulted in Coronavirus Disease 2019 (COVID-19) disease, being globally diagnosed for more than 2 years, while global vaccination strategies are evident for more than a year, now. Yet, there are several possible routes that SARS-CoV-2 can enter into the Central Nervous System (CNS), and also, cross-immunity with myelin has also been discussed (Lima et al., 2020). A study revealed that HERV-W envelope protein was highly expressed in leukocytes of COVID-19 patients and could promote certain pathognomonics of the disease, and to a further extent, it could be a potential biomarker for a severe COVID-19 (Balestrieri et al., 2021). Another study revealed an upregulation in HERVs in children with mild or moderate COVID-19 but a decrease in those with a severe disease (Tovo et al., 2021). However, literature data highlight a possible exacerbation of neurological conditions in cases with COVID-19, and particularly, a recent case series analysis concluded that SARS-CoV-2 infection may affect the MS or even cause a relapse (Finsterer, 2022; Michelena et al., 2022).

A study showed that SARS-CoV-2 RNA can be reverse-transcribed and integrated into the genome of cultured human cells and can be expressed in patient-derived tissues, suggesting that may this evidence explains the long diagnostic tests' true positivity in certain cases (Zhang et al., 2021; Mouliou and Gourgoulianis, 2021). Another recent study found that BNT162b2 mRNA is reverse transcribed intracellularly into DNA, *in vitro* in human liver cell line, and this could raise concerns if BNT162b2-derived DNA is incorporated into the host genome (Aldén et al., 2022).

Temelimab (GNbAC1) is an immunoglobulin (Ig)G4 monoclonal antibody targeting HERW-W protein; this immunotherapy was revealed to have no effect on acute adaptive immune inflammation, although it did show preliminary radiological indicators of anti-neurodegenerative benefits, and current data support that treatment for progressive MS (Hartung et al., 2022). GeNeuro has begun working with leading medical centers in Europe and the United States to evaluate temelimab as a therapeutic treatment, both to prevent immune system hyper-activation in newly infected patients and to treat severe neurological and psychiatric syndromes in patients with long-COVID syndrome.

Combining the facts that many people have been infected with SARS-CoV-2 and that certain cases show prolonged PCR test positivity, several have been vaccinated against COVID-19 and that SARS-CoV-2 may influence MS disease course or clinical emergence, we highlight the need for temelimab to be urgently studied particularly for MS vaccinated and non-vaccinated patients with COVID-19. Although more studies are required to reveal the relationship of COVID-19 and MS exacerbations, current evidence suggests a potential linkage, thus may different temelimab treatment schedules and dosages are needed. Finally, we highlight the need for the next step after temelimab clinical trials, to consider that the drug will be administered in MS cases that have been vaccinated or non-vaccinated people as well as in those with and without a history of COVID-19, thus the potential drug dosage-efficacy in MS patients could be influenced by these factors.

Funding

None.

CRediT authorship contribution statement

Dimitra S. Mouliou: Conceptualization, Writing – review & editing. **Efthimios Dardiotis:** Writing – review & editing.

Declaration of Competing Interest

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.msard.2022.103938.

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https://doi.org/10.1016/j.msard.2022.103938
Received 22 April 2022; Received in revised form 22 May 2022; Accepted 3 June 2022
Available online 6 June 2022

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