Multiple Sclerosis Disease-Modifying Therapies in the COVID-19 Era

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Introduction

Disease-modifying therapies (DMTs) for multiple sclerosis (MS) influence the immune system in many ways. It is necessary to understand how these medications might impact susceptibility to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and/or whether they are associated with more severe coronavirus disease 2019 (COVID-19) for clinical decision-making and patient counseling. In this webinar, the American Neurological Association (ANA) interviewed three academic MS subspecialists: Dr Elena Grebenciucova at Northwestern University, Dr Brandon Moss at Cleveland Clinic, and Dr Scott Newsome at Johns Hopkins. The panel discussed emerging data from national and international registries of MS patients with COVID-19, and key patient and DMT characteristics to consider when making clinical decisions during the pandemic, including expected impacts on immune responses to an eventual SARS-CoV-2 vaccine.

Interpreting MS/COVID-19 Registry Data

The panelists agreed that in the early days of the COVID-19 pandemic, there was appropriate concern regarding management of MS patients, especially those on higher efficacy therapies. We are now fortunate to have a wealth of data from patient registries, including the active COVID-19 Infections in MS & Related Diseases (COViMS) registry in North America, which has now collected information on >900 patients with MS and related neuroimmunologic conditions.[1] Based on these data, the panelists agreed that there does not appear to be a significantly increased risk of severe COVID-19 in those receiving a particular DMT. Characteristics of an individual's disease associated with increased risk of mortality include significant disability (requiring assistive devices or being nonambulatory) and a progressive MS subtype. Other risk factors in MS patients have been largely consistent with the general population, such as older age and medical co-morbidities, including diabetes and hypertension. This is consistent with data published from similar registries in France and Italy,[2,3] although Dr Grebenciucova cautioned on extrapolating these data to a Western population with significantly higher rates of co-morbidities, such as obesity. More data are needed to generate stronger conclusions, and clinicians are encouraged to submit cases in North America to the COViMS registry at www.covims.org.

Factors to Consider in DMT Decision-Making during the COVID-19 Pandemic

All panelists agreed that adequate and effective treatment of MS should remain the primary consideration in DMT decision-making. Dr Newsome emphasized the importance of weighing the chance of contracting COVID-19 and having a bad outcome against the chance of having a bad outcome from MS, given the risk of permanent disability in those who are

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undertreated. In most patients, the panelists are continuing pre-pandemic treatment strategies owing to this risk.

However, there are additional factors to consider when making clinical decisions during the pandemic. Dr Grebenciucova referred to the impact of immunosenescence in older MS patients, whose CD8 T cells might have reduced ability to respond to a pathogen, thus leaving them at higher risk of viral infection or of suboptimal response to vaccination. The panelists also expressed caution during the pandemic in starting cell-depleting therapies that affect the immune system broadly and have a prolonged duration of effect, and they suggested a strategy of temporizing with a lower-risk DMT in the appropriate setting. For those already on highly efficacious DMTs, such as natalizumab or ocrelizumab, extending the dosing interval might be appropriate in those with less pre-infusion disease activity or in those with progressive disease, in whom the potential benefits might be less.

Dr Moss commented in his recent observational study that the main risk factor for developing suspected or confirmed COVID-19 was a known history of exposure, highlighting the importance of standard infection prevention measures.[4] In patients who have been stable on a DMT for a prolonged period, delaying routine magnetic resonance imaging for disease surveillance might help to avoid exposure. Occupations that might put patients at higher risk for COVID-19 (eg, medical professionals) and local COVID-19 prevalence are additional factors to consider.

Potential Effects of DMTs on a SARS-CoV-2 Vaccine

As we get closer to a vaccine against SARS-CoV-2, the impact of DMT on vaccine responses has been a frequent topic of discussion. As Dr Moss highlighted, much of the existing evidence for DMTs and vaccine responses focuses on protein-based vaccines, and it is challenging to extrapolate these data to some vaccine types under consideration for SARS-CoV-2, such as viral vector and mRNA platforms. Nonetheless, the panelists agreed that there is concern regarding the impacts of cell-depleting therapies, such as ocrelizumab, on rates of seroconversion and seroprotection after vaccination based on data from the VELOCE study.[5] For those on immune reconstitution therapies (cladribine, alemtuzumab, or stem cell transplant), similar concerns exist during the cell-depletion phase but are likely to be minimized after immune reconstitution.

For new starts, highly efficacious DMTs, such as natalizumab, might be preferred over cell-depleting therapies in the appropriate patient, at least until after vaccination and an immune response are achieved. For those currently on B cell-depleting DMTs, delaying infusions to allow some degree of B cell repopulation is an option, especially in those who have been receiving these DMTs for ≥2 years. Although a recent study suggested that extended dosing intervals with rituximab is still effective,[6] the present uncertainty surrounding the timing of vaccine availability makes it difficult to design a vaccination strategy around levels of B cell suppression. Regardless, the panelists agreed that patients on B cell-depleting therapies should still get vaccinated. These patients should still be able to mount an antibody response to a vaccine (although it might be diminished). A vaccine will still prime T cells, and a vaccine could theoretically boost memory T cells from prior coronavirus exposures.

Other Impacts of the COVID-19 Pandemic on MS Patients

The panelists also acknowledged the indirect impacts of the COVID-19 pandemic on MS patients. Dr Moss pointed out that 16% of patients at the Cleveland Clinic Mellen Center have had an interruption in rehabilitation services during the pandemic.[4] Many have also experienced increased stress, depressed mood, and decreased medical contact during the pandemic, reinforcing the need for clinicians to ask MS patients about other symptoms and medical screenings. Education of patients and family members on MS, DMT risks/benefits, COVID-19, and Centers for Disease Control and Prevention (CDC) guidelines remains crucially important. Patient and family education on vaccine risks and side effects can also mitigate aversion to vaccination.

Suggested Supplemental Material

The full-length version of the webinar can be reached at https://myana.org/education/ana-webinars or via the QR code:

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Author Contributions

J.R.C. was responsible for the concept of the webinar, conducted the interview, and drafted the commentary. E.G., B.P.M., and S.D.N. participated in the interview and editing process.

Potential Conflicts of Interest

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