Looking ahead: the future of MS management Q&A

Day 1

Douglas Sato and Céline Louapre

Debate: COVID-19 will improve the future management of patients with MS

Q: Are virtual consultations a disadvantage for older patients who may not be as comfortable with technology?

A: Douglas Sato – Older patients may require their family's support to perform online visits. However, after a few consultations, many have learned how to operate the computer/mobile apps and also started to use the chat and other fast communication tools like WhatsApp and Telegram.

A: Céline Louapre – This is not my experience. I have experienced problems with patients who have cognitive impairment. Where online visits were not doable because of computer/smartphone/tablet issues, or because the patient did not know how to use such equipment, phone calls were also possible, although this is not a good option for new patients.

Q: Do you think that the pandemic will increase psychiatric comorbidities? What are your recommendations for your patients?

A: Douglas Sato – Yes, we are facing an increase in anxiety and depression, as well as suicide attempts. Patients need to monitor their mental status by checking their performance and pleasure in their daily activities, changes in sleep, eating, excessive alcohol drinking, as well as their adaptation to work and social distancing. They should inform their doctor when they feel that something is wrong, so he/she can evaluate whether any treatment or adaptation is required.

A: Céline Louapre – I agree that there is an increase in anxiety and depression in the MS population as well as in the general population, and results are starting to be published on this topic (e.g. Stojanov A *et al. Mult Scler Relat Disord* 2020;45:102407). The best advice is to stay in touch with their general practitioner, neurologist, and physiotherapist to continue to exercise.

Ide Smets and José Flores-Rivera

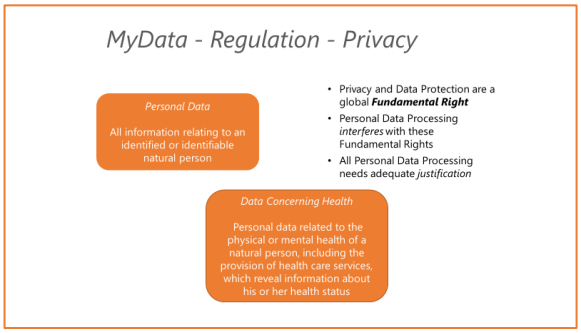
The role of digital health in reshaping MS medical services

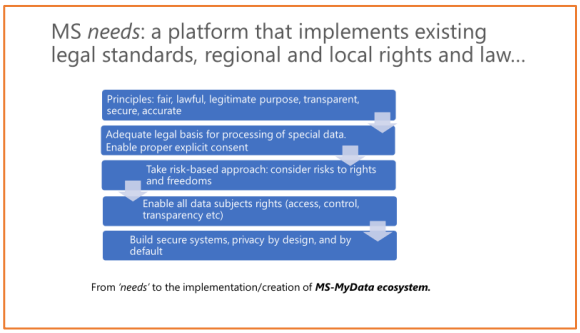
The role of digital health in improving MS monitoring and research

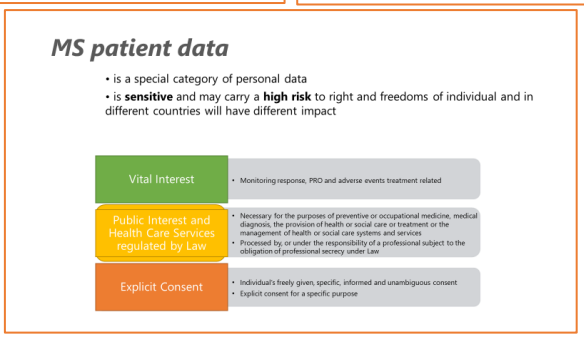
Q: How would you make the most of patients' data while also protecting the data and patient's privacy?

A: Ide Smets – We use official NHS platforms to conduct the remote clinics that operate in line with all privacy regulations. Furthermore, all patient-related data are logged into our CRS system as if it were a face-to-face clinic. In the context of obtaining consent for study participation, the ethical committee has approved several consent forms in which patients can digitally sign (for example, by filling out their email address).

A: José Flores-Rivera –







Saúl Reyes Niño and Lana Zhovtis Ryerson

Debate: Should patients with MS be vaccinated against COVID-19?

Q: What should the lymphocytic count be when you will give the COVID vaccine?

A: Lana Zhovtis Ryerson – My threshold will be an absolute lymphocyte count of 200 based on a vaccination study of fingolimod (Kappos L *et al*. *Neurology* 2015;84:872–879).

A: Saúl Reyes Niño – Ideally, the absolute lymphocyte count should be above the lower normal limit. Among those who are lymphopenic (and extrapolating from the HIV/cancer literature), a CD4 count of 200 cells/μL may be a suitable cut-off value below which vaccination should not be given.

Q: Would you still recommend the COVID vaccine if it provided the same efficacy compared to a strain of bad match seasonal flu vaccine and did not provide a decrease in severity of COVID infection (because even a bad flu virus match still provides some benefit to patients who receive the vaccine)?

A: Lana Zhovtis Ryerson – I am hopeful that the current vaccine studies which show they are 90% (Pfizer) and nearly 95% (Moderna) effective are adequate to induce a protective immune response in patients. However, as for all risk–benefit analyses, vaccines need to be contemplated and we have to be assured that people with MS are not at higher risk of molecular mimicry-like reactions.

A: Saúl Reyes Niño – Assessment of the efficacy of a vaccine is complex for many reasons but particularly so in the case of a novel pathogen (of which our understanding is evolving). Protection against severe disease is one of the most important efficacy endpoints for COVID-19 vaccine efficacy but it is difficult to assess in phase 3 clinical trials. We will have to wait for large phase 4 trials or epidemiological studies done after widespread COVID-19 vaccine introduction to more accurately address this endpoint. Research has shown that random genetic drift, rather than adaptive selection, can explain the rare SARS-CoV-2 mutations. Viral diversity has challenged vaccine development efforts for other viruses such as influenza; however, influenza constitutes a more diverse population than SARS-CoV-2 viruses. SARS-CoV-2 viruses that are currently circulating constitute a homogeneous viral population. We can therefore be cautiously optimistic that vaccines in current development would likely match all currently circulating variants (Dearlove B *et al*., 2020;117:23652–23662). I would recommend the COVID-19 vaccine as long as we are sure that it has a favourable safety profile, even if efficacy is not 100%. Some protection is still better than none.

Q: Do you see a role for checking antibodies after a vaccine (particularly if multiple-dose vaccine(s) are approved)?

A: Lana Zhovtis Ryerson – I am not sure that antibodies will be helpful here, given the fact that the neutralizing antibody response varied significantly, with some patients generating very high titres and about 30% of the patients failing to develop high levels (including 10 patients with undetectable levels) of neutralizing antibodies (Wu *et al*., *JAMA Intern Med* 2020; 2020;180(10):1356–1362). Some factors that may account for discrepant results have been discussed (*N Engl J Med* 2020;383:1694–1698) in response to the study of Ibrarrondo *et al*., 2020 (Ibarrondo FJ *et al. N Engl J Med* 2020;383:1085–1087). Furthermore, T-cell response immunity possibly may be a more important factor, because studies have shown that SARS-CoV-2 induces robust memory T-cell responses in antibody-seronegative and antibody-seropositive individuals with asymptomatic or mild COVID-19 (Gallais *et al*., 2020 https://doi.org/10.1101/2020.03.30.20047365; Nelde *et al*., *Nat Immunol* 2020; Velay *et al*., *J Diag Micro Bio* 2020).

A: Saúl Reyes Niño – I totally agree with Lana. I would only add that there are currently no immune correlates of protection for SARS-CoV-2 or other coronaviruses that affect humans. Therefore, it is unclear what titre of antibodies is sufficient to confer protection against infection.

Q: Would you advocate for a registry for safety for people with MS and safety (across all DMTs)?

A: Lana Zhovtis Ryerson – I think that this issue is important and I would definitively advocate for a registry for safety for people with MS.

A: Saúl Reyes Niño – I would also advocate for such a registry, especially for patients on maintenance immunosuppressive DMTs and immune reconstitution therapies, for whom little or no evidence exists on the safety and efficacy of other vaccines.

Day 2

Sharmilee Gnanapavan

Should we be targeting intrathecal plasma cells to treat MS?

Q: How do anti-CD20 therapies act on cells trapped in follicles?

A: The anti-CD20-mediated B-cell depletion is most likely taking place in the peripheral blood. The therapies can target germinal centre B cells as well, suggesting that it is possible. Antibodies can get into the CNS, but I do not know if they can directly target the cells in the CNS follicles.

Q: Do you think we will see an increase in MS diagnoses in the future based on what we see with Epstein–Barr virus, as a result of coronavirus infections/long COVID?

A: The incidence of MS is rising but the cause is multifactorial and not likely related to one thing. There has not been a spike in MS diagnosis since the first SARS-CoV1 or MERS epidemic, although with SARS-CoV2 there are CNS inflammatory presentations, but this is more for acute disseminated encephalomyelitis than MS. Difficult to say.