Q&As from the *triMSx* meeting 'Managing multiple sclerosis during the **COVID-19 pandemic**' on 30 April 2020

It should be noted that this information was provided for the *triMSx* meeting on the 30 April 2020. Given the fast-paced developments with the COVID-19 pandemic, we would advise you to use up-to-date guidance relevant to your own situation.

It should also be noted that this document mentions the use of unlicensed medicines and medicines used outside their indication. Prescribers should consult local prescribing information.

Professor Marco Salvetti

Q. Why is there a lack of autopsy data in patients with COVID-19?

A. For several reasons. The first reason is the emergency situation, and the second reason is for biosafety issues. However, some data do exist (for example, data that have allowed us to understand the link between COVID-19 and thromboembolism).

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Professor Tony Cunningham

Q. Would you recommend seasonal vaccination in patients with MS during the COVID-19 pandemic?

A. Yes indeed for influenza. It will reduce the load on hospitals during winter. Patients over 65 years of age should have the high dose or adjuvanted vaccines.

Q. Should we test patients using DMTs in the future for COVID-19 in cases of symptoms of acute respiratory infection?

A. If they have respiratory symptoms, which could be COVID-19, then definitely yes, especially if they are on immunosuppressive drugs like fingolimod or alemtuzumab. In Australia, we would test patients whether they are on DMTs or not because we have enough tests and want to suppress outbreaks.

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Associate Professor Tomas Kalincik

Q. Should we consider stopping anti-CD20 agents in the context of future benefit from a vaccine against COVID-19?

A. We are yet to see whether the IgM and IgG responses to COVID-19 are (a) protective and (b) sustained. Given the uncertainties about the role of the serological response and the effectiveness of the future vaccines, it would be premature to stop anti-CD20 therapies.

Q. What is the reason for classifying natalizumab as a moderate-risk therapy?

A. The proposed risk stratification is based purely on the immunological response to COVID-19 infection and on the mechanisms of action of MS drugs. Natalizumab does not interfere with the immunological response to COVID-19 and would therefore be expected to be of moderate risk. Epidemiology data are to follow.

Q. Given that there are ongoing studies on the use of fingolimod as a treatment for COVID-19, could DMTs (apart from cladribine and alemtuzumab) help to protect patients with MS from COVID-19?

A. This is uncharted territory. We have yet to see evidence regarding this question. A trial using fingolimod in patients in intensive care with COVID-19 was underway in late April.

Q. Increasing evidence suggests that SARS-CoV-2 is a neurotrophic virus. In this case, do you still consider natalizumab a 'low-risk' agent?

A. As highlighted above, the proposed risk stratification is based purely on the immunological response to COVID-19 infection and on the mechanisms of action of MS drugs. Natalizumab does not interfere with the immunological response to COVID-19 and would therefore be expected to be of moderate risk. Epidemiology data are to follow. However, a valid point is that if COVID-19 eventually proved to be neurotrophic, then it would be important to understand whether a sufficient immune response can be mounted by the mononuclear cells and CD8+ T cells behind the blood–brain barrier.

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Professor Eva Havrdová

Q. After delaying ocrelizumab for several months, what B cell cut-off should be used to restart ocrelizumab?

A. It is not necessary to check B cells, just treat again as soon as possible.

Q. For patients with highly active MS who need a second dose of alemtuzumab during the pandemic, would the delay of the second dose affect the effectiveness of the agent? How long could the second dose of alemtuzumab be postponed?

A. We sometimes have to postpone a second pulse of alemtuzumab because of infection or unplanned pregnancy, but it does not seem to affect the effectiveness of the agent. However, this has not been studied directly. Therefore, administer the second pulse when the local situation is acceptable and ensure that the patient is compliant with all necessary precautions concerning the pandemic.

Q. Should we postpone alemtuzumab treatment until we have a vaccine?

A. Definitely not.

Q. Could DMTs for MS be used to prevent ARDS?

A. A recently published study from Hong Kong shows that a combination of interferon beta-1b combined with antivirals (remdesivir) used after several days of symptoms (not too late and not in severe patients) may lead to accelerated recovery; therefore, it seems yes, they could be used to prevent ARDS.

Q. For how long can we postpone the administration of cladribine?

A. As necessary until the risk of MS reactivation outweighs the risk of infection.

Q. Would you escalate DMT now in a patient who has radiographically active disease only (i.e. no clinical activity but 10 new or enlarging lesions), despite use of natalizumab for the past 6 months?

A. If natalizumab is not effective, I would not call it escalation but a switch – in this case ocrelizumab could be safe if you exclude progressive multifocal leukoencephalopathy, but you may consider delaying this approach by 1–3 months (while, of course, taking the risk of clinical attack into account).

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Associate Professor Anneke van der Walt

Q. What level of surveillance during the COVID-19 pandemic would you suggest for patients with MS receiving alemtuzumab before the second dose?

A. I would suggest delaying the second cycle of alemtuzumab, if possible. If the second cycle does go ahead, I would like the person being treated to have a normal lymphocyte count. In addition, a period of self-isolation for the first 4–6 weeks after the dose would not be a good idea. However, advice will definitely vary between countries and neurologists and is dependent on the person's own circumstances and the local risk of contracting COVID-19. The treating team should discuss these with the patient.

Q. Is extended-interval dosing (EID) in natalizumab-treated patients being recommended for all treated MS patients during the pandemic?

A. It is one option to consider. The efficacy of EID of natalizumab has not been conclusively established but, for instance, the impression from retrospective studies is that the duration of effect could be linked to body weight. EID could be considered in situations where infusion resources are limited or hard to access.

Q. Would an extended-interval dosing (EID) approach with S1P modulators, akin to natalizumab, by dosing every other day for example, be of use?

A. The lymphocyte count in people on S1P modulators like fingolimod and siponimod takes quite some time to increase on complete cessation of the treatment. In my opinion, alternative daily dosing of these treatments is unlikely to alter the risk of contracting COVID-19 or having a more severe infection.

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Dr Liesbet Peeters

Q. Are there other data banks that propose to achieve the same aim as yours (MS Data Alliance)? If so, will you be sharing data with each other?

A. Yes, the Global Data Sharing Initiative is not a database registry or cohort, but aims to achieve joint insights across the different initiatives, so we can scale up as fast as possible.

Q. When may we see the first insights from the MD Data Alliance data?

A. We hope to present our insights as soon as possible. The first results are expected in mid-May. The progress of the initiative is updated every week on www.qmenta.com

Notes from delegates:

1. Dr Peeters has already mentioned several MS-COVID registries. I would like to add the Spanish MS-COVID registry under the auspice of the Spanish Neurological Association, which has final data on more than 75 patients with MS and confirmed COVID-19 infection.
2. We have data from the Scottish MS register linking COVID-19 positive tests with MS. The highest predictor of a positive test is healthcare professional employment - most of these are asymptomatic/not admitted to hospital. We have small numbers, but the system is fully automated and provides a weekly report. I will share more details in the public domain in due course.

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Ms Bernadette Porter, MBE

Q. What are the limitations to the NeuroResponse® service?

A. As highlighted during the meeting Q&A, we had to co-design the platform via telephone and virtual interviews rather than face-to-face, which means we may have missed some aspects of service design valued by patients.

We created our service within 4 weeks of the lockdown announcement, which did not give us enough time to integrate results directly into hospital electronic systems. Therefore, prescribing hospitals receive the results in a PDF format.

Q. How fast can you roll the NeuroResponse® service out to a larger part of the country?

A. With the correct funding secured and agreed governance signed off, we can mobilize the service in other regions within 12 weeks and across the whole country in 8 months.

Q. How many people currently make up the team behind NeuroResponse® and what are their roles?

A. We are a small agile team of clinical, NHSX and NHS Improvement experts. Our delivery partners are large UK providers.

Q. How many people do you see this impacting over the next 6–12 months?

A. Locally, we identified 500 people eligible for the service in the first 4 weeks. The platform is set up with scaling capabilities to support the UK community who use disease-modifying drugs.

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