Immunotherapy for patients with neuroimmunological disorders during the COVID-19 pandemic

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Corona Virus Disease 2019 (COVID-19) is a new illness caused by the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which typically causes fever, cough, respiratory symptoms, diarrhea, reduction of smell and taste sensation and may lead to pneumonia, acute respiratory distress syndrome and in some patients, death. Nearly every country in the world has been affected with this virus and is currently defined as a pandemic by the World Health Organization. There are no known proven therapies for this virus at present.

There is currently no evidence on how COVID-19 affects people with neuroimmunological disorders (including Multiple sclerosis, CNS Vasculitis, Myasthenia gravis, Immune neuropathies, Myositis or autoimmune encephalitis). However, most patients with neuroimmunological disordes are on immunosuppressive or immunomodulatory therapies. Some diseases, especially myasthenia gravis, also causes respiratory muscle weakness, and there is heightened sense of concern for potential risk of infections with this novel coronavirus and the severity of manifestations.

Individuals with neuroimmunological disorders have asked for guidance on the use of therapies during the COVID-19 pandemic. There are now numerous recommendations circulating, especially by national and international societies for distinct diseases, that attempt to provide clarity and guidance. There are differences among the recommendations that have created confusion and immunotherapy decision making varies significantly from country to country, ranging from highly provider-directed to a more collaborative decision-making model.

EAN here provides some general recommendations regarding major questions related to immune therapy and neuroimmunological diseases.

The EAN expert panel* believes that therapy decisions should be individualized and made collaboratively between the person with the disease and his/her healthcare provider.

In general: should immune therapies in patients with neuroimmunological disorders be reduced or stopped?

Immune therapies include IVIG, Corticosteroids, Alemtuzumab, Ocrelizumab, Rituximab, Interferon-beta, Glatiramer acetate, Prednisolon, Dimethylfumarate, Teriflunomide, Fingolimod, Cladribine, Azathioprine, Mycophenolate Mofetil, Cyclosporin A, Methotrexate, Eculizumab, Tocilizumab.

Currently it is unclear whether and how immune therapy per se does increase the risk of SARS-CoV-2 infection.

Immuntherapy belongs in most of the cases to the standard of care for immune-mediated neurological disorders, and cessation can cause disease exacerbation. This risk can be higher than the risk to worsen COVID-19 disease course under current immune therapy.

It is recommended that patients on immunosuppressive medications should practice extra-vigilant social distancing, including avoiding public gatherings/crowds, avoiding crowded public transport and where possible use alternatives to face-to-face consultations (eg: telemedicine). Moreover, good personal hygiene is extremely important, it is recommended to wash oneself hands frequently. If travelling or using public transport is absolutely necessary, it is recommended the use of protective masks and hand sanitizing

Are there specific recommendations for certain types of immune therapies?

Some of the treatments are applied non-continuously, and short-term changes of the regimen might not be reasonable.

Certain infusion therapies (e.g., natalizumab, rituximab, ocrelizumab, alemtuzumab) may require travel to infusion centers and we strongly recommend that this decision be made based on regional incidence of COVID-19 and risk/benefit of the therapy for the individual patient. Your healthcare provider should be able to give you region-specific advice, and where possible consider switching to home infusion.

Sphingosin-1-Phosphat-Receptor-Modulators (Fingolimod, Siponimod) in general are associated with increased risk of respiratory infections, but cessation of therapy is associated with significant risk of disease activity return in MS patients (including rebound activity). Patients should be specifically advised to confine contacts and minimize risks of infection.

Especially for therapies with immune depleting properties or primary immune suppressive agents (especially Ocrelizumab, Rituximab, Cladribine, Alemtuzumab, Mitoxantrone), in the first weeks after their initiation there could be an increased risk of infections. In older patients and patients with comorbidity (cardiovascular, pulmonary), treatment initiation should be delayed (if disease activity allows). For patients with ongoing therapies, timing of retreatment with immune depleting therapies should be revised by consultant and delay in treatment is recommended if possible or consider alternative options.

Intravenous corticosteroid pulse therapies that are provided in the absence of a clear clinical indication or justification should be avoided.

There is currently no evidence to suggest that intravenous immunoglobulin (IVIG) or plasma exchange (Plex) carry any additional risk in catching COVID-19. However, the use of IVIG has to be based on individual patient need and indiscriminate use should be avoided. In general, Plex and IVIG should be reserved for patients with acute exacerbations. However, the panel

recognize that there are some patients receiving these as maintenance therapy, who should continue these, but extra precautions may need to be taken because of the need for travel to and from a healthcare facility.

There is currently no evidence to support the assumption that inhibition of complement using mAb eculizumab increases susceptibility to COVID infection or its outcome.

There is currently no evidence to support the assumption that inhibition of leucocyte traffick with natalizumab increases susceptibility to COVID infection or its outcome.

Some of the immune therapies require frequent blood work monitoring and decision regarding ongoing need for testing which requires patient to leave their home should be individualized and based on regional COVID-19 incidence.

In any case of acute signs of infection, immune therapies must not be initiated or continued, especially immune depleting agents should be delayed until symptoms have disappeared.

What to consider when starting an immune therapy in patients now:

Start of immune depleting therapies

Before starting a cell depleting therapy (e.g., ocrelizumab, rituximab, alemtuzumab, cladribine) healthcare providers should consider the risk of immune suppression and susceptibility to infections up to several weeks after treatment initiation. It may be advisable to delay initiation of cell depleting therapies, until the peak of the pandemic is over in the region. However, in occasional patients the risk of not starting the cell depleting therapy may outweigh the risk of severe COVID-19 infection and this has to be discussed with the patient in detail. Also the potential of “bridging therapy” concepts has to be discussed with the patient in detail.

How to deal with patients in ongoing clinical trials?

Currently, there are numerous ongoing clinical trials in several neuroimmunological diseases and we strongly recommend that any decision regarding ongoing need for in-person evaluations and treatments under the clinical trial be based with consideration for patients’ best interest. In clinical trials also the sponsors responsibility and communication regarding study protocol continuations has to be considered.

Is there reasonable evidence for medications treating COVID 19?

Various medications have been mentioned in the news and social media as being useful to treat COVID-19 (e.g.,chloroquin, azithromycin, anti-virals, etc). However, these are not proven to be effective at this time. Patients should be aware that some of these medications can potentially worsen MG and should avoid using these without specific medical approval.

Whether anti-Il-& receptor mAb (tocilizumab, sartralizumab), natalizumab or eculizumab are useful as treatments of COVID-19 pneumonia is currently unclear. Several clinical trial are now underway to explore the potential of distinct modes of action in this serious condition (for further informations see clinicaltrials.gov).

Should neuroimmunological patients go for vaccinations?

Vaccinations can protect for a variety of infections/pathogens. However, in the current situation it is recommended to only use dead vaccines in this patient group. For the actual corona virus there is no vaccine available.

We are continuing to monitor this quickly evolving situation and these recommendations may be modified as data becomes available.

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