



Highlights from the 8th ECTRIMS Focused Workshop

"The Risk of Infections for MS Disease Modifying Treatments (DMTs)"



Paediatric MS

Dr Yael Hacohen, UCL, London, United Kingdom

Paediatric MS is rare, particularly in pre-puberty. Therefore, due to the limited number of reported cases, it is difficult to assess a causal relationship between the use of immunosuppressive or immunomodulatory treatments and the development of infections. Four clinical cases are presented to highlight some key considerations for children affected by MS under disease modifying treatments (DMTs): the lack of a consensus on the correct dosage to be used in terms of efficacy and safety, other observed immune-mediated complications (i.e. hypogammaglobulinemia and lymphopenia) than B-cell depletion that can arise from the use of biologic medications, longer treatment duration with more DMTs, and the impact of environmental risks on the likelihood of developing infections for those children. No direct complications have been observed from Covid-19, except reduced compliance to treatments during home schooling, which has led to an increase in the number of relapses. In addition, paediatric MS patients under immunotherapies seem to take longer to clear from Covid-19 and this may interfere with their clinical management. Because of the rarity of paediatric MS, international collaborative cohort studies and phase 4 clinical studies could provide new insights to improve the clinical management of paediatric MS patients.



Pregnant Women

Dr Ruth Dobson, QMUL, London, United Kingdom

Very little data is available to guide practice on immunosuppression or immunomodulation during pregnancy in women affected by MS. The knowledge about the immunology of pregnancy is still relatively poor: overall, the first trimester appears to be pro-inflammatory, the second trimester a tolerogenic immune state, and the third trimester again immune active to prepare child birth. Maternal infections during pregnancy are common, including urinary tract infection, listeriosis, non-respiratory viral infections, varicella and other herpes viruses infections. All of these infections may lead to adverse pregnancy outcomes and, in some reported cases, an increased risk of infections has been associated with immunosuppression treatments. Impact of maternal infections during pregnancy can be on the mother, but many mild or self limiting infections may also have adverse outcomes on the baby. Several of the infections are

vaccine preventable or treatable, highlighting the importance of vaccination pre-pregnancy. In women under DMTs, time of vaccination is key, as there could be an attenuation of vaccine response in individuals receiving anti CD-20 therapy. In addition, the potential impact of immunosuppression during pregnancy is not negligible on neonatal infections and infant vaccine response. Covid-19 infection rates and clinical syndromes seem to be similar in pregnant women compared to non-pregnant women.



The Role of Comorbidities and Advanced Age on the Risk of Infections

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Aging is associated with quantitative and functional changes in the immune system, known as immunosenescence. Low-grade inflammatory state is a key component of immunosenescence. In MS patients a general loss of immune capacity associated with age is observed; not surprisingly, the risk for infection-related hospitalizations increases markedly with age. Higher risk for infections in aged individuals affected by MS can be related to the use of DMTs that may accelerate the immunosenescence process. Changes in immune cell number and function due to DMTs can be detrimental to the already compromised immune capacity in the aging population (i.e. higher risk of PML, cryptococcal infection, and VZV reactivation). Limited data are available on comorbidity and risk of infections associated with DMTs use, but studies in other autoimmune populations suggest that comorbidities may increase the risk of infections. More research is needed to evaluate comorbidity and safety of DMTs, as well as the concomitant effects of aging and comorbidity (and other factors like smoking).



Infectious Risks in Specific Populations: Latin America

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The prevalence of MS in Latin America is low, probably thanks to a combination of genetic and environmental protective fac-



tors. A minor latitudinal gradient in MS frequency seems to exist between different Latin American countries, which could be explained by regional-specific ethnic and environmental contributors. MS treatments in Latin America do not differ from international recommendations, but access to DMTs is a limiting factor in many countries. Post-marketing studies and real-world evidence data of using some DMTs in Latin American populations have demonstrated a similar efficacy and safety compared to international clinical trials, but scarce information is available with respect to risk of infections. A general increase in opportunistic infections including tuberculosis has been observed in Latin American MS patients under DMTs, thus leading a local expert panel to edit some recommendations for screening of infections in MS patients planning to start a DMT. In Latin American MS patients affected by Covid-19 older age and longer disease duration have been associated with poor clinical outcomes. Overall, more information needs to be gathered on the frequency and risk of infectious complications in Latin American MS patients.



Infectious Risks in Specific Populations: India/Asia

Dr Lekha Pandit, Centre for Advanced Neurological Research, Nitte University, India

Multiple sclerosis is considered as an orphan disease in India, because of its low prevalence. "Off label" therapies like immunosuppressants are more affordable in a low income setting and therefore used as first line treatments rather than DMTs. Most of the routinely used immunosuppressants in India are not lymphocyte depletors, thus the risk of infections is expected to be lower compared to other therapeutic options. Interferon Beta and Glatiramer Acetate are the first line in female patients with childbearing potential, while Dimethyl Fumarate is the preferred choice if there are no childbearing issues. Rituximab is used as second line treatment. The screening protocol before patients start treatment includes mandatory serology and lymphocyte count, chest X-ray, USG abdomen, and CIC training for urinary infection, among other examinations. Blood and urine tests are routinely repeated every 3 months during treatment. Data from a small Indian cohort of MS patients show a non-significant difference in terms of infections between different therapeutic agents and compared to non-treated patients. Infections were manageable and often mild. The Covid-19 pandemic did not negatively impact the management of MS patients under treatment.