No simple or uniform solutions exist to improve stroke care worldwide.[5] Disparities among countries constitute a major barrier when evaluating the implementation of programmes to reduce the burden of stroke.

Quality improvement strategies would be an effective approach to account for differences across countries and improving patients' experiences in stroke care.[8,9] The US Agency for Healthcare Research and Quality recommends a sequence of steps known as the Deming cycle or Plan, Do, Study, Act (PDSA). One of its major advantages is the customisation of programmes and strategies according to each country needs and available resources.[10] The PDSA cycles become iterative by using the achievements as the starting point to tackle the next goal and priority.

As a result of the mentioned concepts, we should not expect simple solutions from partners working in isolation, but should work together (clinicians, researchers, policy makers, and academic institutions) towards the common UN goals of embracing country collaborations to reduce premature death caused by non-communicable diseases by improving prevention and treatment, and to promote mental health and wellbeing. We paraphrase an African proverb to highlight the impact of teamwork: "If you want to go fast, go alone. If you want to go far, go together". Physicians and policy makers have to work together towards better access and delivery of stroke care services in Latin American countries and worldwide.

*Gustavo Saposnik, *Vladimir Hachinski*
Division of Neurology, Department of Medicine, and Outcomes and Decision Neuroscience Research Unit, Li Ka Shing Knowledge Institute, St. Michael's Hospital, University of Toronto, ON, Canada (GS); and Department of Clinical Neurological Sciences, Western University, London, ON N6A 5A5, Canada (VH)
vladimir.hachinski@lhsc.on.ca

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Immune checkpoint blockade for treating progressive multifocal leukoencephalopathy

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A case series from the National Institutes of Health[1] and two single case-reports[2,3] indicate that some cases of progressive multifocal leukoencephalomyelopathy (PML) can benefit from treatment with pembrolizumab or nivolumab, which are anti-programmed death protein 1 (PD-1) checkpoint-blocking antibodies.

PML is a severe opportunistic brain infection caused by neurotropic variants of the John Cunningham (JC) virus, a ubiquitous polyoma virus latently present in up to 50% of the adult healthy population.[4] PML usually occurs in the setting of immunosuppression (eg, in haematopoetic malignancies and lymphoma, HIV infection, and in patients treated with immunosuppressive drugs). Neurologists have become highly alerted to PML as it is the most common and serious complication of natalizumab, a monoclonal antibody used for treating multiple sclerosis. For natalizumab-associated PML, discontinuation of the immunosuppressive therapeutic antibody is the pragmatic first step in treating the opportunistic infection.[5] However, for PML associated with other conditions it is impossible to withdraw the causative agent. In such cases it would be desirable to stimulate the immune system by other means.

Immune checkpoint blockade with monoclonal antibodies has emerged as a very promising strategy for treating various malignancies. This approach also has potential for the treatment of chronic infectious diseases such as malaria, HIV infection, hepatitis B, and tuberculosis.[6]

Immune checkpoint-blocking antibodies bind to inhibitory molecules expressed on immune cells, allowing the immune system to fight the JC virus infection. The checkpoint-blocking antibodies pembrolizumab and nivolumab bind to the PD-1 molecule, a negative immune regulator that is upregulated on activated T cells.[6] PD-1 has two physiological ligands, PD-1 ligand 1 (PD-L1) and PD-L2, which are displayed on a variety of cell types, including antigen-presenting cells and some tumors. When PD-1 binds to its ligands, the T cell expressing PD-1 progressively loses function and eventually can become permanently exhausted. The proportion of cytotoxic T cells that express PD-1 and are JC virus-specific is elevated in patients with PML, indicating that T-cell exhaustion can contribute to the pathogenesis of PML.[7] These observations provided a convincing rationale for exploring immune checkpoint-blocking antibodies for the treatment of PML.

The case series from the National Institute of Health included eight patients who were treated with one to three infusions of pembrolizumab.[1] The patients had different underlying conditions, including chronic lymphatic leukemia, non-Hodgkin lymphoma, idiopathic lymphopenia, and HIV infection. Of these eight patients, five (63%) improved or stabilised, two (25%) deteriorated, and one (13%) did not show any clinical, radiological, or virological response. The two (25%) patients with HIV-associated PML had been on effective anti-retroviral therapy and had undetectable HIV viral load (blood and CSF), yet they were progressing without clinical or radiological evidence of immune reconstitution syndrome before pembrolizumab was started. They both stabilised or improved after pembrolizumab treatment.

The accompanying case reports describe one patient with idiopathic primary immunodeficiency whose PML improved after treatment with nivolumab,[2] and one patient with common variable immunodeficiency complicated by diffuse large cell B-cell lymphoma and chemotherapy whose PML responded to pembrolizumab.[3]

Together, these observations indicate that immune checkpoint-blocking antibodies can be a useful therapeutic option for some patients with PML. Checkpoint-blocking antibodies have a substantial risk of adverse effects, notably drug-induced autoimmune reactions.[8,9] In the National Institute of Health case series, recurrent skin rashes, which occurred in two (25%) patients, were recorded as the only notable therapy-associated adverse reactions. As stated in the accompanying editorial,[10] the reports are encouraging but more data and experience are needed to further define the efficacy and risk profile of immune checkpoint blockade in PML with different underlying conditions.

Reinhard Hohlfeld
Institute of Clinical Neuroimmunology, Ludwig Maximilians University, D-81377 Munich, Germany; and Munich Cluster for Systems Neurology, Munich, Germany
reinhard.hohlfeld@med.uni-muenchen.de

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β-secretase inhibitors for Alzheimer's disease: heading in the wrong direction?

The global effort to decipher the molecular basis of Alzheimer's disease and develop disease-modifying treatments, which began in the mid-1980s, has accelerated in the last several years. Genetic, neuropathological, biochemical, and human biomarker analyses all suggest an early role for accumulation of the amyloid β protein