is not captured by the modified Rankin Scale. For this reason, we believe that the inclusion of all intraparenchymal haemorrhages can give new insights into the neurological management of patients who have had endovascular therapy. Beyond the association of haemorrhagic infarction type 1 and type 2 after endovascular therapy withoutcome, the latter haemorrhagic lesions might substantially change medical management (ie, there is a wide range of intraparenchymal haemorrhage types, possibly limiting the initiation of antithrombotic treatments after endovascular therapy). With the perspective of new antithrombotic strategies to be tested to improve reperfusion, the question as to whether a blood pressure strategy could have an effect on all intraparenchymal haemorrhages after endovascular therapy becomes highly relevant.

Beyond this debate regarding the primary endpoint (ie, considering or not all intraparenchymal haemorrhages), we believe that the BP-TARGET trial has highlighted important issues in the blood pressure field, especially for future randomised trials. For instance, which modality should be used to monitor blood pressure in the acute phase (ie, invasive or not), and which blood pressure threshold should be targeted (lower or individualised)? More importantly, is blood pressure after endovascular therapy a prognostic marker rather than a therapeutic target? As future randomised controlled trials will consider the modified Rankin Scale as a primary outcome, we believe that the BP-TARGET trial can provide complementary and additional insights to answer these important questions.

MM declares consulting activities for Boehringer Ingelheim, Amgen, Air Liquide, and Acticor Biotech. All other authors declare no competing interests.

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Published **Online** July 5, 2021 https://doi.org/10.1016/S1474-4422(21)00213-1

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Off-label use of aducanumab for cerebral amyloid angiopathy

The anti-amyloid β monoclonal antibody aducanumab was approved on June 7, 2021, by the US Food & Drug Administration (FDA) for the treatment of Alzheimer's disease.[1] Approval was provided under the FDA's accelerated approval process for drugs that treat serious conditions and fill an unmet need, and was based on the surrogate endpoint of reduction of amyloid β plaques in the brain.

The FDA approved aducanumab specifically for Alzheimer's disease, and noted in its prescribing information that "the safety of ADUHELM [aducanumab] in patients with any pre-treatment localized superficial siderosis, 10 or more brain microhemorrhages, and/or with a brain hemorrhage greater than 1 cm within one year of treatment initiation has not been established".[2] US physicians will nevertheless be able to prescribe aducanumab off-label for the related condition of cerebral amyloid angiopathy (CAA). Similar to Alzheimer's disease, CAA is thought to be triggered by accumulation of amyloid β deposits in the brain, occurring in cerebral small arteries, arterioles, and capillaries, with consequent intracerebral haemorrhage and vascular brain injury. As leaders of the International CAA Association, and as clinicians and investigators in the CAA field, we believe that there are substantial uncertainties and concerns about both the safety and efficacy of aducanumab in patients diagnosed with CAA.[3] We therefore believe aducanumab should not be used for the purpose of treating CAA outside the context of a research trial.

From a clinical efficacy standpoint, anti-amyloid β immunotherapy—though a rational approach to CAA that we believe should continue to be explored—has not been shown to provide benefit. Cerebrovascular amyloid β deposits appear more resistant to antibody-mediated clearance than plaque deposits and might be worsened by mobilisation of solubilised plaque amyloid into the perivascular spaces where CAA occurs.[4] The one immunotherapy trial of the anti-amyloid β antibody ponezumab in patients with CAA found a trend towards reduced rather than enhanced cerebrovascular reactivity following three monthly infusions.[5] There is therefore no evidence of beneficial disease modification for anti-amyloid β immunotherapy in patients with CAA to date.

The concern from a safety standpoint is the potential of CAA to promote the amyloid-related imaging abnormalities (ARIA) that have emerged as the major adverse events in trials of aducanumab and other antibodies in Alzheimer's disease. The presence of advanced CAA, inferred by markers, such as cerebral microhaemorrhages or the *APOE* ε4 allele, appears to increase the likelihood of ARIA.[4] CAA is postulated to promote ARIA by compromising perivascular amyloid clearance pathways and by providing a target for direct antibody-mediated attack on amyloid β-laden vessels. The incidence of ARIA in patients with CAA given aducanumab

would therefore be predicted to exceed the substantial incidence observed in Alzheimer's disease trials (35% of patients with Alzheimer's disease who received the full 10 mg/kg aducanumab dose had brain oedema [ARIA-E], and 21% patients had microhaemorrhages and superficial siderosis [ARIA-H]), according to the FDA prescribing information.[2]

In the absence of evidence supporting efficacy, and the existing evidence suggesting increased risk of ARIA, aducanumab should not be considered as a treatment option for disease modification of sporadic or hereditary CAA. We strongly discourage the off-label use of aducanumab for these disorders outside of any future clinical trial.

SMG has served on safety monitoring committees or as a consultant for Alzheimer disease immunotherapy trials done by Washington University, Biogen, and Roche. CC has served as a consultant on cerebral amyloid angiopathy for Biogen. JAS has served as a consultant for Alnylam. EES has served as a consultant on cerebral amyloid angiopathy for Biogen and Alnylam. SJvV has served as a consultant on cerebral amyloid angiopathy for Biogen. AV has served as a consultant on cerebral amyloid angiopathy for Biogen and Alnylam, and has served on safety monitoring committees for Alzheimer Disease immunotherapy trials done by Roche. DJW has served as consultant on cerebral amyloid angiopathy for Alnylam. MAvB and MMV declare no competing interests. Massachusetts General Hospital, the University of Calgary, Lille University Hospital, and University College London participated in the cerebral amyloid angiopathy immunotherapy trial of ponezumab under clinical research support agreements with Pfizer. The University of Calgary participated in an Alzheimer Disease immunotherapy study of aducanumab under a clinical research support agreement with Biogen.

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World Brain Day 2021: a call to stop multiple sclerosis

The World Federation of Neurology (WFN) celebrates World Brain Day on every July 22, focusing on a different theme each year.[1] As highlighted in your Editorial,[2] the theme for this World Brain Day is "Stop Multiple Sclerosis" (video), and the WFN is working jointly with the Multiple Sclerosis International Federation (MSIF), as well as with clinicians and experts affiliated with advocacy organisations throughout Asia and Oceania, Europe, Africa, and the Americas. Many public awareness programmes and educational and social media activities are promoting the movement to stop multiple sclerosis, commencing July 22, 2021, and continuing until October, 2021.

Multiple sclerosis can occur at any age, but the mean age of diagnosis is 32 years—a time when many people are planning to have a family and are building careers. The impact of diagnosis on affected individuals and their families can be profound. Currently, there is no cure for multiple sclerosis, which means that people live with the disease for many decades. Effective disease-modifying treatments are in use and can reduce the disabling effects appreciably, but costs preclude access for many people.

World Brain Day 2021 provides an opportunity to highlight the urgent need for early diagnosis and advocate for access to health care, education, and research, and, most importantly, access to effective treatments that can substantially reduce disability. We have compiled five key messages for multiple sclerosis on World Brain Day 2021 (panel).

We invite neurologists, neuroscientists, health professionals, trainees, technologists, advocacy bodies, patient support groups, and other activists to become part of the 2021 World Brain Day campaign. You can participate by posting our banner

***Panel:* Key messages for World Brain Day 2021**

Disability
Multiple sclerosis can be a debilitating neurological disease that affects every aspect of a person's life, with effects ranging from cognitive impairment to substantial physical disability.

Prevalence
Globally, about 2·8 million people have multiple sclerosis.[3]

Education
We must work with health-care professionals to recognise the signs and symptoms of multiple sclerosis so people can be diagnosed early and treated effectively.

Access to treatment
Disease-modifying treatments slow disease progression, dramatically improving the quality of life for those living with multiple sclerosis, yet access to these medications is unavailable in many parts of the world.

Advocacy
We can help stop multiple sclerosis by diagnosing people earlier, providing better access to life-changing treatments, and advocating for improving the quality of life for those living with the disease and their caregivers.

Published **Online** June 21, 2021 https://doi.org/10.1016/S1474-4422(21)00200-3

For more on **The World Federation of Neurology** see https://wfneurology.org/

See **Online** for video

For more on the **Multiple Sclerosis International Federation** see https://www.msif.org/

For more on the **epidemiology of multiple sclerosis** see https://www.atlasofms.org/chart/united-kingdom/epidemiology/average-age-people-start-to-develop-ms