In children with multiple sclerosis, teriflunomide tempers lesion growth

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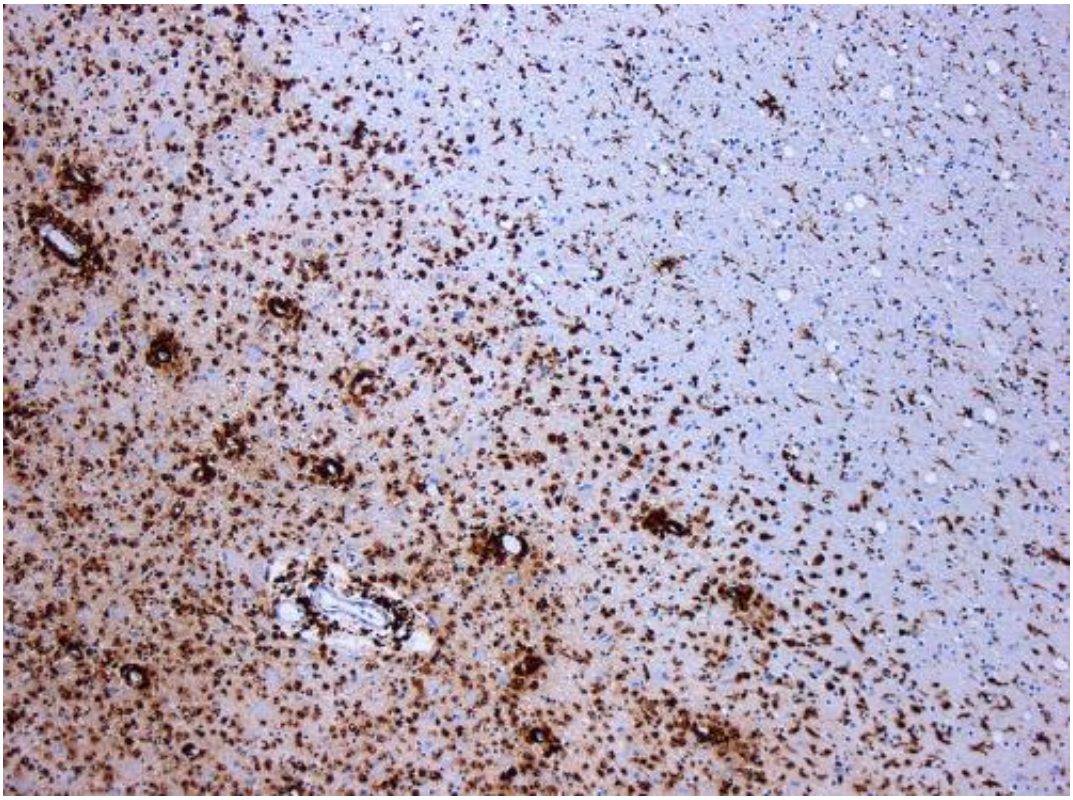

Demyelination by MS. The CD68 colored tissue shows several macrophages in the area of the lesion. Original scale 1:100. Credit: CC BY-SA 3.0 Marvin 101/Wikipedia

There are few treatment options for children with multiple sclerosis—a condition in which the immune system attacks the protective covering of nerves in the brain and spinal cord—and most therapies for the disease

have not been tested in children. An international team of investigators, including researchers at Massachusetts General Hospital (MGH), has conducted a phase 3, randomized, double-blind clinical trial to examine the safety and efficacy of teriflunomide, an oral immunomodulatory drug approved in more than 80 countries for the treatment of adults with relapsing forms of multiple sclerosis. Based on the trial's results, which appear in *Lancet Neurology*, teriflunomide was recently approved by the European Commission for children aged 10–17 years with a diagnosis of relapsing remitting multiple sclerosis.

In the trial, called TERIKIDS, 109 children were randomized to receive teriflunomide and 57 were randomized to receive placebo for up to 96 weeks (nearly two years). Early entry in an open-label extension phase (where patients were guaranteed to receive teriflunomide) was possible before the end of the double-blind period for patients who experienced a relapse or demonstrated high disease activity on MRI imaging tests. Importantly, more patients in the placebo group entered the open-label extension phase (because of high MRI activity) than anticipated, with 26% of patients switching from placebo to teriflunomide before 96 weeks.

After 96 weeks, there was no difference in time to first clinical relapse of multiple sclerosis with teriflunomide compared with placebo. Teriflunomide was well tolerated—serious adverse events occurred in 11% of patients in the teriflunomide group and 11% of patients in the placebo group. Nasal inflammation, upper-respiratory-tract infection, hair loss, tingling sensations, abdominal pain, and increased blood creatine phosphokinase (a marker of muscle damage) were more frequent with teriflunomide than with placebo.

"The trial did not meet its primary endpoint—delaying time to the next clinical relapse—possibly because of more frequent switches to the open-label arm due to high MRI activity. However, the study did meet several

key secondary endpoints related to teriflunomide's ability to reduce the number of new or enlarged lesions that are detected through MRI, suggesting that the medication might have beneficial effects in children with relapsing forms of multiple sclerosis," says lead author Tanuja Chitnis, MD, director of the MGB Pediatric Multiple Sclerosis Center at MGH.

Chitnis notes that an ongoing open-label treatment extension study is continuing to evaluate the long-term effects of teriflunomide in young patients.

Chitnis is also director of the Translational Neuroimmunology Research Center at Brigham and Women's Hospital and a professor of neurology at Harvard Medical School.

More information: Tanuja Chitnis et al, Safety and efficacy of teriflunomide in paediatric multiple sclerosis (TERIKIDS): a multicentre, double-blind, phase 3, randomised, placebo-controlled trial, *The Lancet Neurology* (2021). DOI: 10.1016/S1474-4422(21)00364-1

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