New version of old multiple sclerosis drug performs well in clinical trial

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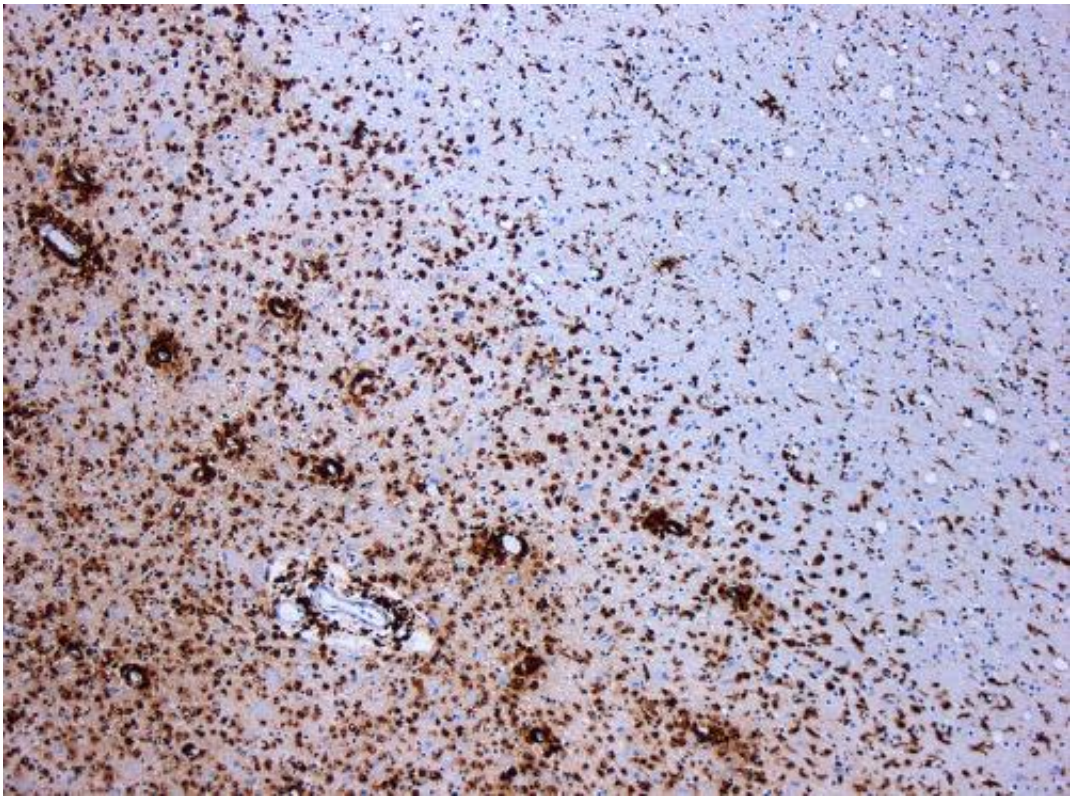

Demyelination by MS. The CD68 colored tissue shows several macrophages in the area of the lesion. Original scale 1:100. Credit: CC BY-SA 3.0 Marvin 101/Wikipedia

Tests of a new long-acting version of one of the oldest multiple sclerosis (MS) drugs on the market show it worked significantly better than placebo in reducing the number of patient relapses and developments of

new or active lesions, researchers report. Most important, they add, the updated version was effective even though injections were given every two weeks instead of every other day, and it appears that fewer patients develop resistance to it.

The industry-funded, international clinical trial led by a Johns Hopkins scientist found that pegylated interferon beta worked far better than placebo for people with the most common form of MS. The beneficial effects seen in this study were comparable to what was found in previous studies in which the standard formulation of interferon beta (which must be taken more frequently) was compared to placebo.

In a report on the trial, published May 1 in *The Lancet Neurology*, the researchers say they also found that while roughly 20 percent of MS patients typically develop antibodies against the drug that ultimately neutralize its effects, fewer than 1 percent in the new study did, suggesting far more patients could benefit from the new formulation.

"While this isn't a brand new blockbuster drug, I do think it will improve compliance and tolerability and therefore positively impact the quality of life of people with MS who take interferon beta," says study leader Peter A. Calabresi, M.D., a professor of neurology at the Johns Hopkins University School of Medicine. "If it gets FDA approval, this new formulation would allow patients to get the same effect, but instead of the burden of injecting themselves every other day, they only have to do it twice a month. For an MS patient, that's a huge advance."

"The data are very, very clear," Calabresi adds. "We can make things easier for our patients without dangerous side effects just by tweaking what we know to be a safe, 20-year-old drug."

MS is considered an autoimmune disorder, caused when the immune system wrongly attacks a person's own tissues; in this case, it's the fatty

protein myelin sheath that insulates nerves that send electrical signals to control movement, speech and other functions. The immune system primes so-called T cells in the body's lymph nodes, preparing them to seek out and destroy myelin, a process that can lead to debilitating symptoms such as blurred vision, weakness and numbness.

In 1993, interferon beta became the first drug federally approved for MS because of its ability to block certain types of immune cell activation and the trafficking of immune cells into the brain. While some studies suggest its effects are modest in controlling MS, Calabresi says it works very well in some patients, overall reducing relapses by one-third and inflammation as measured using MRI by more than two-thirds.

Side effects trouble many patients—including flu-like symptoms that tend to occur in the six to eight hours after each injection—but Calabresi says the drug is safer for routine care than some newer oral medications.

Calabresi says his team was eager to test the new formulation, because many MS patients forego its benefits because of the frequent injection schedule and side effects.

The new version modifies interferon beta by attaching polyethylene glycol (PEG) polymer chemical chains that stabilize the drug. PEG has been proven safe in other medications, shampoos, toothpaste and moisturizers.

For the study, researchers recruited more than 1,500 subjects with MS from 183 sites in 26 countries. For a year, one-third of patients got a placebo shot every two weeks, one-third got 125 micrograms of pegylated interferon beta shots every two weeks and the third group got 125 micrograms of pegylated interferon beta-1a once a month, with a placebo shot given at every other visit.

After a year, those who got pegylated interferon beta-1a every two weeks experienced a 36 percent reduction in the yearly relapse rate compared to the placebo group; the every-four-week group saw a 28 percent reduction. MRI scans revealed 67 percent fewer new or active lesions in the two-week group, while those injected every four weeks only had 28 percent fewer of those lesions.

Both the two- and four-week groups had 38 percent reduction in disability progression on a scale that measures walking speed, vision, strength and sensation, as compared to a placebo group.

The new formulation appeared just as safe as the older one, though Calabresi says that the flu-like symptoms from the long-acting drug lasted closer to 24 hours after each injection in some patients. He called this a trade-off his patients would deem worthwhile.

Data presented April 29 at the American Academy of Neurology suggests that receiving pegylated interferon beta every two weeks is the best dosing schedule.

Provided by Johns Hopkins University School of Medicine