

Discontinuing Disease-Modifying Therapy in Multiple Sclerosis: Should You Have an Exit Strategy?

Two experts sound off on the implications of indefinite treatment and whether DMTs should be stopped.

With Robert Naismith, MD and John Corboy, MD

When selecting treatment for patients with multiple sclerosis (MS), physicians must weigh efficacy and safety along with patient histories and preferences. As the therapeutic landscape expands, choosing a disease-modifying therapy (DMT) that satisfies the goals of treatment is a significant challenge. During this process, one question tends to hang over the proceedings, even if the physician never addresses it: How long will the patient be on the medicine?

The answer may appear simple. Yet, the notion of an exit strategy is still controversial, particularly in light of very real concerns regarding benefits of DMTs over time, as well as the risk and cost associated with treatment. “With regard to these medications, which people may take for decades, we’ve never significantly asked the question: Is it reasonable to continue indefinitely?” asks John Corboy, MD, Professor and Vice Chair of the Department of Neurology at the University of Colorado. However, according to Robert Naismith, MD, Associate Professor of Neurology at Washington University School of Medicine in Saint Louis, although a proverbial end game is desirable when initiating therapy, there are not enough data showing the potential benefits and risks of discontinuation. “We are lacking adequate evidence-based studies to inform us on who are optimal candidates for discontinuation, when to consider, what are the risks, and how to monitor,” says Dr. Naismith.

“In practice, the only way to know whether patients are getting benefit from therapy would be to discontinue and see if their disease re-activates.”

Changes in MS Over Time

Given the relative lack of data regarding when to stop DMTs, Dr. Corboy believes it is extremely important to consider the long-term implications of both indefinite treatment and stopping treatment. One of the major factors that could influence the conversation about therapy cessation is how MS appears to change over time. “We have a lot of epidemiological data suggesting that the manifestation of the disease changes as the patient ages,” says Dr. Corboy. In general, inflammation appears to decrease over years, and Dr. Naismith points out that MRI activity and relapses become less frequent with increasing age and disease duration. Nevertheless, says Dr. Naismith, “while this is true at

PRACTICAL POINTER

Emerging evidence suggest that therapy discontinuation may be beneficial in patients over the age of 60 with no evidence of disease activity for an extended duration. If considering discontinuation, a new baseline MRI would be helpful for future comparisons and to ensure no activity.

WATCH NOW ON PRACTICALNEUROLOGY.COM



Drs. Corboy and Naismith discussed the question of therapy discontinuation as part of Practical Neurology® magazine's coverage of the 2017 American Academy of Neurology Annual Meeting in Boston. Visit PracticalNeurology.com/MS to watch the interview.

the population level, it is often challenging to translate to the individual patient," says Dr. Naismith. "Many people do not recover fully from a relapse. If an older patient, who was already having trouble with ambulation, were to have a severe relapse with treatment discontinuation, the concern would be further loss of ambulation and independence."

The efficacy of therapeutic interventions also appears to change over time, says Dr. Corboy. "There is quite a bit of data suggesting that as people age, medications become less effective." Despite this, choosing which patients in whom to discontinue therapy remains a major challenge, and Dr. Naismith emphasizes the need for continued inquiry in this area. "We need better studies on sequencing and de-escalating treatment. For someone diagnosed with MS in her 20s, the potential implications include several decades of immunosuppressive treatment," says Dr. Naismith. "Our therapies likely have short-term risks and long-term risks. The field still lacks consensus and critical studies to know if we can step-down therapy, and whether the disease 'burns itself out,'" says Dr. Naismith.

Therapy Discontinuation: Considerations

There are several questions to think about if discontinuation is a possibility, according to Dr. Corboy. "What are the risks of recurrence, or progression of disability? What are the benefits of discontinuation? What is the plan if there is recurrence? How will you monitor off medications?" Dr. Naismith would consider stopping a DMT in patients who are disease activity free for an extended duration—such as five years—for both relapses and new MRI lesions. "I would also consider the treatment, because high efficacy therapy can be associated with return of disease activity," says Dr. Naismith.

Another consideration is the patient's age. "There is emerging evidence that discontinuation may be pos-

"With regard to these medications, which people may take for decades, we've never significantly asked the question: Is it reasonable to continue indefinitely?"

sible in patients over 60, currently on standard-efficacy therapy, who have been without disease activity for an extended number of years," says Dr. Naismith. "I would recommend discussing benefits and risks, not just the risk of disease reactivation, but the possible risks of continuing treatment." Prior to stopping, a new baseline MRI will be helpful for future comparisons and to ensure no activity, according to Dr. Naismith. "I would recommend close medical follow-up with an office visit and repeat MRI at three to six months. I would continue to monitor, with repeat MRI and office visit at six to 12 months, and for a number of years with annual follow-up after that," he observes further. "We do not yet know the clinical implications of a couple new T2 lesions off treatment over the course of a number of years. For those patients who relapse or who have three or more T2 lesions in a year, or one to two or more new gadolinium-enhancing lesions, I would recommend return to therapy."

As treatments with different mechanisms of action become available, Dr. Naismith observes that sequencing is also likely to become a key issue. "Some of our treatments have a biologic effect that lasts far beyond the medicine half-life, with prolonged effects that can even last years," he explains.

Conclusion

As more drugs enter the market (both brand name and generic) and more scientific inquiry is devoted to this topic, Dr. Corboy believes that the discussion of whether to stop treatment with a DMT is "not likely to change unless drugs are developed that show efficacy in aging patients." However, he points out, randomized controlled trials are underway to assess the impact of DMT cessation.

Despite the lack of easy answers, Drs. Naismith and Corboy suggest that physicians should be grappling with the question of DMT cessation while awaiting new data and possible guidelines. "We should expect many emerging concepts as our MS options expand: induction, optimization, escalation, combination, re-treatment, de-escalation, discontinuation," explains Dr. Naismith. ■