WriteClick: Editor's Choice

Editor's Note: Subsequent to the online publication of "The American Academy of Neurology's Top Five Choosing Wisely Recommendations,"[1] WriteClick submissions were received expressing concern about the fourth recommendation: "do not prescribe interferon-β or glatiramer acetate to patients with disability from progressive, nonrelapsing forms of MS." The American Academy of Neurology (AAN) responded that, due to an administrative error, they had not originally contacted the AAN Multiple Sclerosis (MS) Section Executive Committee about this recommendation but had contacted them when they learned of the error. An "Expression of Concern" was published online (http://neurology.org/lookup/doi/10.1212/WNL.0b013e318296f79b) attached to the article. After feedback was received from the AAN MS Section Executive Committee, the AAN provided an updated response. After final evaluation, the Editors determined that no corrections to the AAN article would be necessary.

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THE AMERICAN ACADEMY OF NEUROLOGY'S TOP FIVE CHOOSING WISELY RECOMMENDATIONS

David H. Mattson, Indianapolis; Robert P. Lisak, Detroit; David E. Jones, Charlottesville, VA: As representatives of the MS Section of the AAN, we have major concerns about recommendation 4 of the AAN Choosing Wisely Working Group: "do not prescribe interferon-β or glatiramer acetate to patients with disability from progressive, nonrelapsing forms of MS."[1] Due to an administrative oversight at the AAN, this recommendation was never reviewed by the Executive Committee of the MS Section, contrary to what was stated to have occurred in the Methods. This article is not an evidence-based guideline and should not be construed as such. This is an oversimplified recommendation that we strongly feel needs to be more nuanced. Patients with progressive MS with superimposed relapses can still benefit from these agents, as acknowledged in the text of the article. Progressive patients who are on one of these agents and having no relapses are likely obtaining a partial treatment benefit and should remain on the agent. Progressive patients with gadolinium-enhancing CNS lesions can benefit from treatment.[2] Progressive MS shares pathophysiology with relapsing MS, rendering these labels arbitrary and artificial in clinical decision-making.[3] The treatment of a complex disease like MS requires clinical judgment that cannot be reduced to platitudes.

John R. Corboy, Aurora, CO: Recommendation 4 in the Choosing Wisely article by Langer-Gould et al.[1] suggests that interferons and glatiramer acetate (GA) should not be used in patients with progressive, nonrelapsing forms of MS. This recommendation fails to recognize clear benefits in subsets of both secondary progressive[2] and primary progressive[4] patients, especially in those with history of recent relapse, enhancing lesions on scans, and perhaps mostly, younger progressive patients. In addition, what little evidence that does exist on discontinuation of disease-modifying therapies (DMT) in progressive MS suggests that stopping either interferons[5] or natalizumab[6] may be associated with significant recurrence of disease activity. In reality, there is no large, multiyear study designed to examine whether discontinuation of DMT in MS, in any context, is safe and not associated with significant recurrence of disease activity. As most patients with progressive forms of MS (especially secondary progressive MS [SPMS]) will likely already be on a DMT when a decision is potentially made to not use a DMT, a recommendation to simply not use MS medications is premature and potentially dangerous. This issue requires not only more discussion, but a lot more data.

Author Response: Rod Larson, Minneapolis; Gary Gronseth, Kansas City, KS; Thomas S.D. Getchius, Minneapolis; Annette Langer-Gould, Los Angeles: We apologize for our inadvertent failure to obtain review from the AAN MS Section for the Choosing Wisely recommendations before the AAN Board of Directors approved the list. AAN staff reached out to relevant AAN Sections in August 2012 to review the list of recommendations, and it was an inadvertent error that the e-mail did not reach the MS Section. When we were notified of this omission, we sent the MS recommendation and supporting text to the full MS Section for comment in April 2013. That comment period ended on May 2, 2013, and the AAN's Choosing Wisely Work Group reconvened on May 8, 2013, to evaluate responses and respond to Mattson et al. and Corboy.

Author Response: Annette M. Langer-Gould, Los Angeles; Gary S. Gronseth, Kansas City, KS; Rod Larson, Thomas S.D. Getchius, Minneapolis: We apologize for the error that prevented us from obtaining comments sooner from the AAN MS Section Executive Committee. We solicited feedback from the entire Section. A majority of members fully agreed with the AAN Choosing Wisely Working Group's recommendation 4.[1] Thirty-four percent of the 91 respondents disagreed with the recommendation and raised concerns similar to those of Dr. Mattson et al. and Dr. Corboy. It is important to note that these concerns were not new and had already been brought to the Working Group's attention during the development process by other groups from whom feedback was solicited.[1] The Working Group reconvened and found no reason to change this recommendation. Recommendation 4 is based on strong evidence. Five randomized controlled trials failed to demonstrate any clinical benefit of treatment with interferon-β or GA in patients with progressive, nonrelapsing MS.[7,8] One trial[7] found some decrease in short-term relapse-related disability; thus, we carefully worded the recommendation to focus on nonrelapsing forms.

Drs. Mattson et al. and Corboy raise an important issue: patients with progressive, nonrelapsing MS with gadolinium-positive lesions might benefit from immunomodulating therapy. This assertion is supported by a subgroup analysis of a study of rituximab in patients with progressive, nonrelapsing MS.[4] However, despite the high proportion of patients with gadolinium-positive lesions in trials of SPMS,[7] neither interferon-β nor GA has been reported to reduce relapses in the nonrelapsing, gadolinium-positive subgroup.[2,8]

Expecting cessation of interferon-β or GA to accelerate clinical deterioration in patients with progressive, nonrelapsing MS at treatment initiation contradicts the evidence showing no slowing of disability progression. In addition, expecting the use of interferon-β or GA to be responsible for complete relapse cessation (despite disability progression) in patients with SPMS (who by definition had relapses at some point in the past) is inconsistent with the evidence showing only a modest reduction in MS relapse frequency and is more likely attributable to the natural history of SPMS. In contrast, although not specifically studied, a beneficial effect of continued interferon-β treatment in patients with progressive, relapsing MS who have remained free from relapse and disability progression seems plausible.

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4. Hawker K, O'Connor P, Freedman MS, et al; OLYMPUS trial group. Rituximab in patients with primary progressive multiple sclerosis: results of a randomized double-blind placebo- controlled multicenter trial. Ann Neurol 2009;66:460–471.
5. Wu S, Dastidar P, Kuusisto H, Ukkonen M, Huhtala H, Elovaara I, Increased disability and MRI lesions after discontinuation of IFN beta-1a in secondary progressive MS. Acta Neurol Scan 2005;112:242–247.
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7. La Mantia L, Vacchi L, Di Pietrantonj C, et al. Interferon beta for secondary progressive multiple sclerosis. Cochrane Database Sys Rev 2012;1:CD005181.
8. Wolinsky JS, Narayana PA, O'Connor P, et al; PROMiSe Trial Study Group. Glatiramer acetate in primary progressive multiple sclerosis: results of a multinational, multicenter, double-blind, placebo-controlled trial. Ann Neurol 2007; 61:14–24.

Author disclosures are available upon request (journal@neurology.org).

The American Academy of Neurology's Top Five Choosing Wisely recommendations

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Neurology 2013;81;1022-1023
DOI 10.1212/WNL.0b013e3182a69c98