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Counseling Patients on Long-term Disease-modifying Therapy



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Counseling Points™

Counseling Patients on Long-term Disease-modifying Therapy

Continuing Education Information

Target Audience

This educational activity is designed to meet the needs of multiple sclerosis (MS) nurse specialists and other nurses in care of patients with MS.

Purpose

To provide MS nurses with strategies for discussing the efficacy and safety of continuous treatment for MS, while tailoring the management approach to best fit the individual patient's needs.

Learning Objectives

Upon completion of this educational activity, the participant should be able to:

- Discuss the benefits of long-term therapy for patients with multiple sclerosis (MS)
- Summarize current long-term data as a basis for discussing the efficacy and safety of continuous treatment for MS
- Identify reasons for discontinuation of disease-modifying therapy (DMT) in MS, including reasons for switching therapies
- Develop strategies to help patients maintain their therapy and optimize its efficacy benefits in managing MS

Continuing Education Credit

This continuing nursing education activity was approved by the Wisconsin Nurses Association Continuing Education Approval Program Committee, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.

This activity has been approved for 0.8 contact hours.

Approximate time to complete this activity is 0.8 hours.

This program expires June 30, 2012.

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welcome

Dear Colleague,

Much of the professional education in multiple sclerosis (MS) has focused on getting patients to start disease-modifying therapy (DMT), but equally important is educating patients about the benefits of *staying* on therapy over the long term. The need for long-term therapy can present a significant challenge for the MS nurse and an understandable source of concern for the person with MS. Patients may question: “Is this therapy really helping me?” or wonder, “Why can’t I take an occasional ‘holiday’ from my medication?”

Nursing professionals need solid strategies for discussing the efficacy and safety of continuous treatment for MS. This year, new data have become available to help establish the long-term efficacy and safety profile of available DMTs for MS. This includes data from 15 years of continuous therapy with glatiramer acetate and 15-year follow-up data from patients on intramuscular interferon beta-1a. A key goal in this issue of *MS Counseling Points™* is to help summarize current data in a way that allows nurses to use it to educate patients with MS.

Staying on an effective therapy is an important way for patients with MS to achieve their best possible outcome and minimize their disability level over the long term. As nurses, we know that often the most effective therapy is the one that the patient can adapt to and use consistently. Factors that influence this are different for everyone; thus, therapy must be individualized for each patient. We hope that this issue of *MS Counseling Points™* will be useful as you guide your patients in this important aspect of MS care.

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Counseling Patients on Long-term Disease-modifying Therapy

Nearly two decades ago, the first patients to use disease-modifying therapies (DMTs) for relapsing-remitting multiple sclerosis (RRMS) were essentially pioneers. The agents they were taking for MS were new and unproven; their safety records unknown. Patients and MS care practitioners took a gamble with the key questions of “Are these treatments safe?” and “How do we know if they work?”

Today, we have some answers to these questions and, fortunately, the gamble has paid off for many of the patients who have used DMTs long term and continuously. No significant safety concerns have emerged over 15-plus years of treatment with glatiramer acetate (GA, Copaxone®), interferon beta-1a (Avonex®), or interferon beta-1b (Betaseron®).¹⁻⁴ Expanded Disability Status Scale (EDSS) scores among patients receiving continuous long-term treatment have been significantly lower at follow-up than among those who have stopped therapy or who have been on intermittent therapy; in addition, conversion to secondary-progressive MS (SPMS) has been delayed.¹⁻⁴

Current Long-term Data on DMTs in MS

Controlled trial data do not always mirror the real world of patient care, and following patients for extended time periods presents many logistical difficulties. A primary disadvantage to long-term, open-label trials is the lack of a placebo group or other valid comparator groups. It remains unknown how patients would have fared if they had received no therapy, what happened to those who switched to different therapies, or how the switched group might have done if they had remained on their initial drug. However, looking at the big picture—particularly in comparison to what is known about the natural history of MS—the data demonstrate significant benefits of available long-term therapies.⁵

15-year GA Data in RRMS

The US Glatiramer Acetate Trial is the longest evaluation of continuous immunomodulatory therapy in RRMS.¹ This trial is unique in that it has followed patients who remained on GA therapy as their sole immunomodulating agent—without switching to other drugs or going off therapy—for as long as 15 years.

The US Glatiramer Acetate Trial is the longest evaluation of continuous immunomodulatory therapy in RRMS.

Investigators enrolled 232 patients with RRMS who received at least one GA dose since the study’s initiation (the intent-to-treat cohort). Participants were evaluated every 6 months using the EDSS as the primary measure of disease activity. As of 2008, 100 patients (43%) remained on the study drug (the “ongoing” cohort), receiving an average of 13.6 years of continuous GA treatment.¹ Key efficacy findings released in 2010 are summarized in **Table 1**.

Patients receiving continuous GA therapy (the ongoing group) had a mean disease duration of 22 years and a mean age of 50 years, yet 2/3 did not transition to a secondary-progressive stage of MS during the 15-year period, 57% had stable or improved EDSS scores, and 82% remained ambulatory without the need for mobility aids.¹ The annualized relapse rate (from a baseline of 1.12) was 0.43 in the intent-to-treat cohort and 0.25 in the ongoing cohort. The investigators concluded that long-term treatment with GA delayed accumulation of disability in patients with RRMS as measured by EDSS score and conversion to SPMS, and the patients remaining on this therapy appeared to do better compared with the withdrawn cohort.

Table 1. Efficacy Findings from GA 15-year Study¹

	Intent-to-treat Cohort	Ongoing Cohort	Withdrawn Cohort*
Exposure to drug	8.6 yrs	13.6 yrs	4.8 yrs
Disease duration	17 yrs	22 yrs	13 yrs*
Patients with stable or improved EDSS score	54%	57%	52%*
Time for 25% of patients to reach EDSS 4.0	4.0 yrs	6.8 yrs	2.75 yrs
% reaching EDSS:			
4.0	39%	38%	40%*
6.0	23%	18%	27%*
8.0	5%	3%	6%*

*While on GA therapy.
EDSS=Expanded Disability Status Scale; GA=glatiramer acetate.

The most commonly reported adverse events related to the study drug were local injection-site reactions and immediate post-injection reactions. There was no evidence of new adverse events associated with long-term therapy.

There was no evidence of new adverse events associated with long-term therapy.

The findings of this study cannot be directly compared to those of other long-term studies of DMTs in MS. Differences in trial design include the prospective approach, regular patient follow-up (every 6 months), and the fact that patients remained on the study drug as their sole DMT for the duration of the trial.

16-year Interferon Beta-1b Data

Long-term studies of interferon beta-1b have followed the original pivotal trial participants for up to 16 years after randomization.^{2,3} The follow-up study stratified patients according to their original dose in the pivotal trial (250 mcg, 50 mcg, or placebo) as well as by the length of time they were exposed to the study drug (<10%, 10% to 80%, or >80% of the time since the start of the trial). Of the 328 patients identified from

the original cohort, 293 were alive and 253 agreed to participate in the follow-up study. High ascertainment was attributed to efforts by investigators to assist patients with travel to study centers and with home visits and phone interviews for those unable to travel.³ Some of the key data are summarized in **Tables 2 and 3.**²

Patients with higher exposure to the study drug had a slower progression to an EDSS score of 6.0 compared with those who received treatment for shorter periods. In the group with 10% to 80% interferon exposure, 46.9% of patients reached EDSS 6.0. The proportion of patients converting to SPMS was 45%. In this trial, EDSS scores at the start of treatment were predictive of the participants' current disability score—in general, those with lower initial scores had lower scores at the long-term follow-up and vice versa.² The investigators concluded that sustained early treatment can delay progression to significant disability and that improving early disability has long-lasting effects.

The most commonly reported adverse events in the long-term interferon beta-1b trial were injection-site reactions, malaise, flu-like symptoms, headache, fever,

Table 2. Mean Annualized Relapse Rate by Exposure to Long-term Interferon Beta-1b²

Years	Length of Exposure to Study Drug		
	< 10%	10% to 80%	>80%
1 to 5	0.90	0.85	0.59
6 to 10	0.62	0.50	0.40
11 to 16	0.48	0.50	0.28

Table 3. Time from Diagnosis to Confirmed EDSS 6.0 for Patients on Long-term Interferon Beta-1b²

Group	Years
Low exposure	7 years
Medium exposure	10 years
High exposure	13 years

EDSS=Expanded Disability Status Scale.
Long-term Interferon Beta-1b²

and myalgia. No new treatment-related adverse events were seen.²

15-year IM Interferon Beta-1a Data

Also released in 2010 were long-term data on treatment with intramuscular (IM) interferon beta-1a.⁴ This study did not involve regular follow-ups over the 15-year time period, nor did patients remain on the study drug continuously. Rather, this was a single time-point study of 122 eligible, living patients who had completed at least 2 years of IM interferon therapy in the original open-label trial. The long-term evaluation included a group of 56 patients who were currently receiving the study drug (median duration of therapy 13.3 years) and 66 patients no longer on the study drug. Outcomes evaluations were based on EDSS, SF-36, visual analog scale (VAS) scores, and questionnaires about drug history, employment status, and living arrangements. Key findings are summarized in **Table 4**.⁴

Table 4. Percentage of Patients Reaching EDSS Milestones in 15-Year Interferon Beta-1a IM Trial⁴

EDSS Score	Patients on IM interferon	Patients not on IM interferon	P value
4.0	64%	83%	0.062
6.0	32%	62%	0.007
7.0	33%	9%	0.008

EDSS=Expanded Disability Status Scale; IM=intramuscular.

Not all patients in the “current therapy” group had remained on IM interferon over the 15-year period; some had also used subcutaneous interferons (n=16) or GA (n=6). Of those no longer on IM interferon, the most commonly used DMTs were natalizumab (13%) and GA (12%). Twenty-two patients (18%) were not receiving any DMT at the time of follow-up.

After 15 years, patients on the study drug had lower mean EDSS scores, less disability progression over time (EDSS change from baseline), and longer time to EDSS milestones compared with patients not currently on the study drug. Twenty-seven percent remained

progression-free during the study period and 36% progressed no more than two EDSS points. Patients taking the study drug reported better quality of life and were more likely to be living independently.⁴ While safety outcomes were not specifically studied, no new adverse events were identified over the 15-year period.

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What Can Be Inferred from Existing Long-term Data?

The net effect of these trials is to establish to MS health care professionals and patients that existing drugs are safe and effective for extended time periods of 15 years and beyond. Head-to-head comparisons of their results, however, are not valid. Each of the long-term studies described here differs substantially in trial design, outcomes, and baseline characteristics of the subjects enrolled. For example, some of the trials collected data after long intervals during which patients were not monitored and many had discontinued, switched, or added other immunomodulators. Clearly, long-term, placebo-controlled studies in MS are not feasible. Thus, the available data cannot clearly address to what degree the outcomes are related to the therapeutic effect of a drug and how much may be due to differences in the natural history of the disease among individuals.⁶

It stands to reason that patients who remain on a particular therapy over a long-term period would mainly consist of those who perceive a good therapeutic effect from the drug. Greater progression of disability in the control groups and increased rates of switching between agents suggests that more patients in these

latter groups experienced aggressive forms of MS that did not respond as well to standard therapies.^{4,6}

An important function of long-term studies in MS is the accumulation of a large body of safety data. In the studies described here, no unforeseen adverse events emerged with long-term use of any of the platform therapies.¹⁻⁴

In the studies described here, no unforeseen adverse events emerged with long-term use of any of the platform therapies.

Staying on Long-term Therapy: Benefits and Barriers

Success in maintaining long-term therapy for MS is very patient-specific, but much depends upon the quality of education and support provided by the MS care team.⁷ Patients are most likely to discontinue therapy in the first 6 months after treatment initiation.^{8,9} In one study following patients with RRMS for a mean of 4.2 years, 46% of patients had stopped treatment during the course of the study.¹⁰

Treatment Gaps or “Drug Holidays”

Some patients believe they can take an occasional “drug holiday,” and may even be told by a clinician that such breaks are healthy. While limited data exist on the long-term effects of such gaps, the few studies that provide such information suggest that patients staying on therapy continuously fare significantly better over the long term than those who take drug holidays.⁶

For example, in the 16-year trial of interferon beta-1b, patients with less exposure to the drug (10% to 80% exposure) were more likely to reach EDSS 6.0 (46.9% of patients) compared with those who had >80% exposure to the interferon (35.7%) at the 16-year follow-up mark.²

Another study used data from a national managed-care database to examine the effect of treatment gaps on rates of severe relapse in MS. Patients with gaps in

therapy lasting ≥ 90 days had nearly double the chance of having a severe relapse than patients with shorter gaps.¹¹

What Are the Barriers to Staying on Therapy?

Lack of efficacy, side effects, method of administration, and disease-related factors all affect how consistently patients remain on long-term therapy in MS. Adherence and retention rates seen in clinical trials may in fact be higher than in the “real world,” where fewer incentives and less-formalized follow-up and support may contribute to a pattern of switching between therapies or discontinuing therapy altogether.⁷

In addition to knowing what works for an individual patient, understanding when and why people with MS discontinue therapy can help the nurse to provide appropriate monitoring and support. Some of the available facts associated with therapy discontinuation are summarized in **Table 5**.

Perceived loss of or lack of efficacy is one of the most commonly cited reasons for treatment discontinuation.^{12,13} Side effects are another key reason, and

Table 5. Facts About Discontinuation of Therapy⁷

- Patients are most likely to discontinue a DMT within the first 6 months of treatment
- Discontinuation rates in some studies are nearly 50% by the 4-year mark
- Discontinuation rates are thought to be higher in clinical practice than in controlled trials
- Progressive disease course, higher disability level, and more active disease correlate with increased discontinuation rates
- Patients with untreated depression are more likely to discontinue therapy than patients whose depression is treated
- Perceived lack of efficacy is one the chief reasons for discontinuing therapy in MS, along with adverse events and difficulty with the administration method (injection)
- Early discontinuation (within the first year) is more likely to be due to adverse events, while later discontinuation (after 3 years) is more often attributable to treatment failure
- Unrealistic patient expectations about therapy are related to higher discontinuation rates

DMT=disease-modifying therapy; MS=multiple sclerosis.

include injection-site reactions from either interferons or GA and flu-like symptoms associated with interferon therapies. Flu-like symptoms vary among individuals, with many patients reporting that these symptoms decrease after extended treatment periods. In trials of subcutaneous interferon beta-1a, flu-like symptoms were reported by 69% of patients at the 4-year follow-up and by 12% after 8 years of follow up.¹⁴

Ongoing expert support can greatly improve patients' likelihood of remaining on their MS therapy and their overall experience with therapy.

The discomfort and inconvenience associated with injectable drugs is inherently a deterrent to long-term therapy for many people with MS.¹⁵ Some patients are able to incorporate self-injection well into their lifestyles, while others struggle with side effects or simply cannot get used to self-injecting effectively. Physical or cognitive limitations caused by the disease process can further interfere with successful administration.¹⁶ Ongoing expert support can greatly improve patients' likelihood of remaining on their MS therapy and their overall experience with therapy.¹⁷ For example, treating depression in MS has been shown to improve adherence to therapy. In one study, 86% of patients who were receiving treatment for their depression remained on DMT, versus 38% of those with untreated depression ($P=0.003$).¹⁸

Progression or Suboptimal Response? Evaluating Changes in Disease Status

Even with the best possible adherence to an effective therapy, most patients with RRMS eventually exhibit some disease progression, and some will begin to show signs of advancing to a secondary-progressive phase. Signs may include relapses, disability progression, new magnetic resonance imaging (MRI) lesions, and brain atrophy.¹⁹

It can be difficult to distinguish signs of progression from those of a suboptimal response to therapy.

In looking at reasons for breakthrough symptoms or relapses, an initial step should be determining the degree of actual adherence to the current therapy.

Progression of Disease

Signs and symptoms suggestive of progression may be related to multiple factors, especially in a patient with long-standing disease. These include lack of adherence, drug side effects, concomitant conditions, or practical reasons such as loss of insurance coverage for physical therapy. The degree to which DMTs are effective in patients who have stopped having relapses remains an important unanswered question in the field of MS.²⁰ Is the lack of relapses due to disease progression, or to the fact that the therapy is staving them off? Is the patient willing to take a chance on worsening disease if therapy is discontinued? Other methods of intervention may help to support patients at this time, including specialized exercise programs or additional physical therapy support.

Supporting the patient who is experiencing progression of disease while on a DMT can be discouraging for MS nurses, who strive to remain optimistic and encouraging about the potential benefits of therapy. Part of this goes back to setting realistic expectations: while disease progression is likely at some point, this does not necessarily mean that the DMT is not working. Nor is it necessarily a time to change drugs or to give up therapy altogether—although sometimes a change in therapy may be warranted. If the change in clinical status is due to atrophy or other structural damage, adding a new drug or therapy is not going to reverse that, based on what is currently known about MS.²¹ However, if the change in status is due to acute episodes during which the patient is accumulating a greater burden of disease, a change in therapy should be considered.^{22,23} If a patient's condition is related to disease progression, switching therapies may only lead to frustration if no improvement is seen on the new treatment.

Suboptimal Response

A suboptimal response to DMT may appear during the early part of treatment or even after many years of

therapy.²³ It remains unknown why some people with MS respond vigorously to treatment and others have suboptimal or partial responses to available therapies.¹⁹

The definition of a suboptimal response remains a source of debate in the MS community, with much depending on exactly how response to therapy is defined. One model assessed response based on relapse activity, disease progression, and MRI findings with parameters defined as “notable, worrisome, or actionable.”²⁴ The Canadian MS Working Group determined that MRI findings should be used in conjunction with measures of relapse and progression.²⁵ The International Working Group for Treatment Optimization in MS emphasized progression of disease, and recommended modifying treatment when progression was coupled with changes in relapse or MRI.²⁶ Many groups have recommend stepwise therapy: starting patients on a first-line immunomodulatory drug and modifying therapy to other agents as monotherapy or combination therapy if patients exhibit suboptimal response.²⁷

Some generally accepted parameters have emerged in defining a suboptimal response and are listed in **Table 6.**²²

Counseling Patients About Switching Therapies

Strategies for switching or modifying the approach to DMT include changing doses or dosing intervals,

Table 6. Definition of Suboptimal Response to Therapy^{22,23,28}

- Clinical and MRI activity after the initial 6-month to 1-year treatment period
- More than one relapse per year or the failure of a given treatment to reduce the relapse rate from pretreatment level
- Incomplete recovery from attacks or patients with recurrent brainstem or spinal cord lesions (known to be associated with an elevated risk for sustained, severe impairment)
- Significant increase in T2 disease burden while a patient is on therapy

MRI=magnetic resonance imaging.

switching between therapeutic agents, and switching to or adding second-line agents such as a chemotherapeutic agent (cyclophosphamide or mitoxantrone) or natalizumab.²³

For interferons, one strategy explored in clinical trials is to increase the dose or dosing interval of the drug. Two studies (EVIDENCE and INCOMIN) have suggested that this approach may boost the drug’s effect in some patients, although a sustained benefit has not been demonstrated and the approach must be weighed against the potential risks.^{29,30} A number of smaller, nonrandomized trials do not support the benefits of switching among different interferon beta preparations.²³

Because GA and interferons have different mechanisms of action in MS, a patient not responding well to one class may respond to the other. Available data include an open-label study of 85 consecutive patients with RRMS initially treated with interferon beta-1a for 18 to 24 months and switched to GA therapy because of either persistent clinical disease activity (n=62) or intolerance to therapy (n=23).³¹ After switching, patients were followed for a mean of 37 months. For patients switched to GA for efficacy reasons, the mean annualized relapse rate decreased, from 1.32 with interferon to 0.52 with GA ($P=0.0001$). Among patients who switched because of tolerability problems, no significant differences in relapse rate were noted. This was an open-label, nonrandomized study, and thus the findings should be interpreted accordingly. Likewise, patients not responding to GA therapy may also benefit from switching to an interferon. Additional randomized head-to-head studies are underway that may shed more light on this issue.

One reason to switch between classes of drugs is the presence of neutralizing antibodies (NAbs) to interferon therapy. Although the significance of NAbs has been highly controversial, some studies show that persistent, high levels of these antibodies in patients with active MS have been associated with clinical evidence of loss of efficacy. Some experts recommend that patients who exhibit a suboptimal response to

therapy and demonstrate sustained positive NAb titers ≥ 20 may benefit from switching to another class of therapy.^{32,33}

Second-line therapies, which include natalizumab and chemotherapeutic agents, are often considered in cases of suboptimal response or “treatment failure.” Natalizumab is approved for monotherapy in patients with active RRMS when treatment with the platform therapies fails due to either efficacy or tolerability reasons.³⁴ Natalizumab must be administered through the “TOUCH” risk management plan, and an understanding of the risks of serious side effects—such as progressive multifocal leukoencephalopathy (PML)—must be coupled with a high level of vigilance in monitoring. For patients with RRMS and rapidly worsening inflammation, therapeutic immunosuppression with cyclophosphamide or mitoxantrone may be appropriate.^{35,36}

Using a combination of two first-line agents is an approach currently under study. A large-scale Phase 3 clinical trial funded by the National Institutes of Health will compare the combination of interferon beta-1a and GA versus either of these therapies alone, with an estimated completion date in 2012.³⁷

Strategies for Counseling Patients About Long-term Therapy

The MS nurse’s role often involves helping patients set expectations about therapy. That does not mean promising that they will no longer have relapses or that the disease will not eventually progress. No existing therapy can offer these guarantees, and no one can accurately predict which patients will have a more benign course and which ones will have an aggressive one—although a low EDSS score in the first 5 years after diagnosis is somewhat predictive of a less-aggressive course.⁶

The Best Therapy Is the One the Patient Will Take

Some agents are a better choice for some people for a variety of reasons, but experts have argued that any medication that an individual will actually take as pre-

scribed and that gives him or her a sense of getting on with life is often the best choice. This raises a key issue for nurses in helping to make the existing therapies as tolerable as possible for patients and individualizing the therapy according to each patient’s needs.

Helping patients understand their options can be important for their acceptance of therapy, both at initiation and over the long term. Giving people choices may help them feel that they are participating in their care decisions rather than just following orders.³⁸

Monitoring Adherence to Therapy

The MS nurse’s role is often that of monitoring adherence to therapy. Nurses need to ask patients how often they are taking their medications—but the manner in which this subject is approached might make the difference between whether a person is truthful or just says what they think the clinician “wants to hear.”³⁸ An understanding and nonjudgmental approach often works best. Some patients have “creative” ways of altering their dosage regimens, which they may believe still constitutes appropriate adherence. Reviewing some data that show lower relapse rates and disease progression in patients with increased exposure to the drug may be helpful in counseling patients about adherence.

Nurses need to ask patients how often they are taking their medications—but the manner in which this subject is approached might make the difference between whether a person is truthful or just says what they think the clinician “wants to hear.”

Setting Hopeful, Yet Realistic, Expectations

Because there is so much hopeful news in the field of MS right now, it’s possible to lose sight of the need to balance this news with realistic expectations for the patient. One study illustrated how unrealistic expectations about therapy can influence rates of discontinuation: When beginning an interferon regimen, 57% of the patients studied had unrealistic expectations about

their potential for a reduction in relapse rate.⁹ Even after receiving an educational program, 36% of patients continued to have unrealistic expectations of therapy. Interestingly, among the patients who discontinued interferon therapy, 64% of them were in the group with unrealistic expectations despite the education program.

Helping patients with MS set and understand their own expectations is not a one-time event, but an ongoing process as the disease, patients' lives, and the available therapeutic options keep changing. Over time, expectations must be refocused and new strategies tried.

Balancing Risks and Benefits of Future Therapies for MS

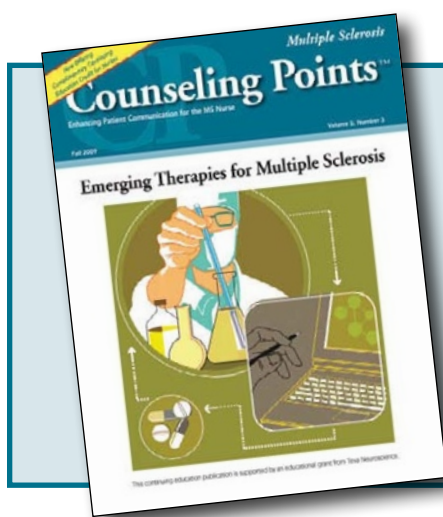
Setting realistic expectations is particularly complicated in today's environment, with all of the "noise" about future, promising therapies for MS. While much of the news is hopeful, at the same time nurses often feel they are "bursting the patient's bubble" by presenting the limitations of a particular treatment strategy. Many MS health care professionals recommend staying the course with current therapies until it is clearer how emerging treatments will affect patients over the long term in regard to both safety and efficacy. For now, patients should be made aware that data from trials of oral agents and monoclonal antibody treatments for MS cannot be compared directly with that of the injectable drugs, due to differences in trial design. That is, we can't compare a 69% and a 39% reduction in relapse rate because of differences in these study populations at baseline.³⁹ Newer therapies will likely involve careful candidate selection and specific programs for monitoring patients for adverse events, which can be more serious than those associated with existing therapies. As newer therapies become available, nurse educators will need reliable sources to help patients weigh the risks and benefits of these therapies relative to the currently available medications.

Talking with colleagues and sharing ideas may help MS nurses to understand that their challenges are not unique. While we want our patients to remain hopeful and optimistic, nurses must be careful to present information in a positive and yet realistic light.

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The following issues of *MS Counseling Points*TM are available at www.counselingpoints.com and www.iomsn.org:

- Update on Clinically Isolated Syndrome
- Emerging Therapies for MS
- Practical Approaches to Spasticity
- Brain Atrophy and Disability in MS

CP Counseling Points™

Counseling Patients on Long-term Disease-modifying Therapy

- Existing disease-modifying therapies (DMTs) have accumulated over 15 years of data with no significant new safety concerns emerging over this time period.
- The US Glatiramer Acetate (GA) Trial followed patients with multiple sclerosis (MS) who remained on GA as their sole immunomodulating agent for up to 15 years.
- Long-term interferon beta-1b studies followed pivotal trial participants up to 16 years, stratifying them according to the original drug dose and length of time they were exposed to the study drug.
- The 15-year study on intramuscular interferon beta-1a was a single time-point study of eligible, living patients completing at least 2 years of therapy in the original open-label trial.
- Long-term trials have shown less disability progression over time (Expanded Disability Status Scale [EDSS] change from baseline), longer time to EDSS milestones, and delayed conversion to secondary-progressive MS compared with patients who did not remain on the study drug.
- Results from the recently published 15-year and 16-year trials cannot be viewed in the same way as those from randomized, placebo-controlled trials because of the lack of comparator groups and differences in study design.
- Patients staying on therapy continuously appear to fare significantly better over the long term than those who take drug holidays.
- Perceived lack of efficacy is a chief reason for discontinuing therapy in MS, along with adverse events and difficulty with the administration method.
- Cases involving apparent lack of efficacy should be explored further to determine possible adherence problems, progression of disease, impact of neutralizing antibodies, and suboptimal response to therapy.
- For patients with suboptimal response, strategies include changing doses, switching between therapeutic agents, and switching to or adding second-line agents.
- Helping patients with MS set realistic expectations is an ongoing process as the disease, the patient's life, and available therapeutic options change.

Counseling Points™

Counseling Patients on Long-term Disease-modifying Therapy

Continuing Education Posttest

To receive contact hours, please read the program in its entirety, answer the following posttest questions, and complete the program evaluation. A certificate will be awarded for a score of 80% (8 correct) or better. A certificate will be mailed within 4 to 6 weeks. There is no charge for the CE credit.

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Via the Web: Applicants can access this program at the International Organization of MS Nurses' website, www.IOMSN.org. Click on Counseling Points and follow the instructions to complete the online posttest and application forms.

PLEASE SELECT THE BEST ANSWER

- In the 15-year trial of glatiramer acetate (GA), patients with multiple sclerosis (MS) in the ongoing group:**
 - took either GA but could switch to another disease-modifying therapy (DMT)
 - took GA as the sole immunotherapy for the trial duration
 - took GA for the first 2 years of the trial
 - stopped therapy when they reached a disability status score of 6.0
- Long-term trials of DMTs for MS have revealed new adverse events, which developed after years of exposure.**
 - True
 - False
- In the long-term trial of interferon beta-1b, patients were stratified according to:**
 - number of enhancing lesions
 - severity of MS at baseline
 - years of exposure to the study drug
 - all of the above
- Long-term data show that patients who remain continuously on DMTs for MS have:**
 - fewer relapses
 - delayed time to disability status milestones
 - less change from baseline in disability status
 - all of the above
- Reasons why long-term trial data must be interpreted with caution include all of the following EXCEPT:**
 - trials do not enroll people with clinically definite MS
 - differences in trial design and baseline patient characteristics
 - heterogeneity of the disease
 - lack of placebo and other comparator groups
- Drug "holidays" are an accepted way to give patients a needed break from long-term therapy.**
 - True
 - False
- Barriers to staying on long-term DMT for MS are:**
 - related to side effects
 - related to the administration method (injectable)
 - related to a lack of efficacy or a perceived lack of efficacy
 - all of the above
- The definition of suboptimal response to therapy includes:**
 - any acute relapse of MS while on therapy
 - more than 1 relapse per year or failure to reduce the pretreatment relapse rate
 - more than 2 relapses per year or failure to reduce the pretreatment relapse rate
 - any sign of change in relapse rate from pretreatment levels
- Switching a patient to a different DMT should be considered in all of the following circumstances EXCEPT when a patient:**
 - has a suboptimal response to therapy
 - tolerates the medication poorly
 - is hoping to halt MS progression
 - shows evidence of neutralizing antibodies to interferon therapy
- Efficacy rates for emerging therapies (e.g., oral therapies) for MS cannot be compared directly with those seen in early pivotal trials of existing therapies because of:**
 - differences in patient populations at baseline (e.g., earlier stage of disease)
 - differences in the pharmacokinetics of these drugs
 - poor recordkeeping in early pivotal trials
 - low likelihood that new therapies will achieve approval status

Counseling Points™: Program Evaluation Form

Counseling Patients on Long-term Disease-modifying Therapy

Using the scale provided, Strongly Agree = 5 and Strongly Disagree = 1, please complete the program evaluation so that we may continue to provide you with high quality educational programming. Please fax this form to **(201) 612-8282**.

5 = Strongly Agree 4 = Agree 3 = Neutral 2 = Disagree 1 = Strongly Disagree

At the end of this program, I was able to: *(Please circle the appropriate number on the scale.)*

- 1. Discuss the benefits of long-term therapy for patients with multiple sclerosis (MS) 5 4 3 2 1
- 2. Summarize current long-term data as a basis for discussing the efficacy and safety of continuous treatment for MS..... 5 4 3 2 1
- 3. Identify reasons for discontinuation of disease-modifying treatment (DMT) in MS, including reasons for switching therapies 5 4 3 2 1
- 4. Develop strategies to help patients maintain their therapy and optimize its efficacy benefits in managing MS 5 4 3 2 1

The following were disclosed in writing at the start of this educational activity:

- 5. Notice of requirements for successful completion Yes No
- 6. Conflict of interest Yes No
- 7. Disclosure of relevant financial relationships and mechanism to identify and resolve conflicts of interest..... Yes No
- 8. Sponsorship or commercial support Yes No
- 9. Non-endorsement of products Yes No
- 10. Off-label use..... Yes No
- 11. Expiration date for awarding contact hours Yes No

Please refer to page 2 for Continuing Education Information.

General Comments

- 12. Time required to complete the educational activity: _____ (minutes)
- 13. As a result of this continuing education activity (check only one):
 - I will modify my practice. (If you checked this box, how do you plan to modify your practice?) _____
 - I will wait for more information before modifying my practice.
 - The program reinforces my current practice.

Suggestions for future topics/additional comments: _____

Follow-up

As part of our continuous quality improvement effort, we conduct post-activity follow-up surveys to assess the impact of our educational interventions on professional practice. Please check one:

- Yes, I would be interested in participating in a follow-up survey.
- No, I would not be interested in participating in a follow-up survey.

There is no fee for this educational activity.

Posttest Answer Key	1	2	3	4	5	6	7	8	9	10

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