Comparative efficacy of alemtuzumab and established treatment in the management of multiple sclerosis

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Abstract: Alemtuzumab is the newest disease-modifying therapy approved for the treatment of relapsing multiple sclerosis. Alemtuzumab is an anti-CD52 targeted antibody that causes lysis of T and B lymphocytes, monocytes, natural killer cells, macrophages, and dendritic cells. Following its administration, a prolonged T-cell lymphopenia results with emergence of a reconstituted immune system that differs in its composition from that pretreatment. In clinical trials, alemtuzumab has shown impressive efficacy with regard to clinical and radiological outcomes in relapsing multiple sclerosis, along with sustained long-term beneficial effects, and it is attractive for its once-yearly administration. Despite this, the occurrence of serious secondary autoimmune disorders, infections, and a potential risk of malignancy necessitates a careful evaluation of risks versus benefits for an individual patient prior to its use. The requirement of patient commitment to the intense mandatory monitoring program is also a factor to be considered when incorporating alemtuzumab into the treatment regimen.

Keywords: alemtuzumab, multiple sclerosis, comparative efficacy

Introduction
Multiple sclerosis (MS) is an autoimmune disorder characterized by inflammation, demyelination, and neurodegeneration.1,2 The first disease-modifying therapy for MS was approved in 1993, and there have since been nine other treatments approved in the USA and Europe, including, most recently, the approval of alemtuzumab by the US Food and Drug Administration (FDA) in November 2014.3–5

Traditionally, first-line agents for the treatment of MS have included interferon β (intramuscular 1a, subcutaneous 1a, and subcutaneous 1b) and glatiramer acetate. Natalizumab and fingolimod have generally been used when patients fail one or more of the above agents; however, with growing experience of their use, albeit less commonly, they are being used as the first agent in patients with highly active disease at onset as well.6 Although the injectable therapies have well established long-term safety data, the inconvenience of injections, the side effects associated with their use, and adherence to the treatment regimen continue to be detriments to their use.4 If increasing experience with the three approved oral medications (fingolimod, teriflunomide, and dimethyl fumarate) establishes their sustained clinical efficacy and long-term safety profiles, their use as first-line agents would be expected to expand in the coming years. The use of alemtuzumab at present will likely be reserved for patients with highly active disease who fail other agents.

Importantly, all medications are approved for the treatment of relapsing MS. Clinical trials have demonstrated efficacy in the relapsing forms of MS, but...
Unfortunately have not shown therapeutic benefit in progressive forms of the disease.\textsuperscript{7,8} Results of therapeutic trials in primary progressive MS have been disappointing.\textsuperscript{9,10} With regard to secondary progressive MS, optimal treatment of the relapsing phase early in the disease seems to have the greatest impact in determining the course of the secondary progressive phase rather than escalating therapy in the secondary progressive stage.

There is increasing interest in the concept of a “therapeutic window of opportunity in MS”. Accumulating evidence points to the benefits of early treatment and the presence of a window of opportunity in which to treat patients in order to have a meaningful impact on long-term disability.\textsuperscript{4,9,10} Disability in the relapsing phase of the disease seems to depend predominantly on focal central nervous system inflammation, while permanent disability in the progressive phase depends on neurodegeneration rather than on ongoing inflammation, and the most important factor determining the rate of progression seems to be the time taken to reach onset of the progressive stage.\textsuperscript{4} Experience from prior trials and clinical practice, including an early trial with alemtuzumab, demonstrated that even if effective suppression of inflammation is achieved in the progressive phase, this does not necessarily translate to halting or slowing disease progression.\textsuperscript{11} Thus, the opportunity to treat patients may come early in the disease before the second degenerative phase is reached.\textsuperscript{10,12,13}

The importance of early optimal treatment as discussed in the preceding paragraph necessitates utilization of early prognostic indicators in deciding the best treatment for an individual patient. Although no specific biomarker that might accurately predict long-term outcome has been identified, several studies have looked at early clinical and magnetic resonance imaging (MRI) features that might indicate the subsequent disease course. Among early clinical features that help make an early determination are: frequency of relapses within the first 2–5 years, incomplete recovery from the first attack, and involvement of the motor and brainstem as possible features of patients deserving aggressive treatment.\textsuperscript{11,14–16} MRI features that might help include the baseline T2 lesion volume, early brain atrophy, number of gadolinium-enhancing lesions, and particularly the change in T2 lesion volume early in the disease course despite being on disease-modifying therapy.\textsuperscript{15,17}

Given this scenario of expanding treatment choices, a better understanding of disease mechanisms in MS, and greater need for early initiation of appropriate and optimal treatment, we aim to review the newest drug, alemtuzumab, try to decipher the role that it can play in the current treatment algorithm, and provide patient-focused perspectives on its use.

**Mechanism of action of alemtuzumab and other agents approved for MS**

Increasing knowledge and better elucidation of the pathological inflammatory processes that occurs in MS has led to the development of many immunomodulatory therapies in recent years. Table 1 lists the agents currently approved by the FDA and their postulated mechanisms of action. Current therapies target immune cell survival, proliferation or behavior in the periphery, as well as transmigration of the cells across the blood–brain barrier.\textsuperscript{18} The newest member of the repertoire is alemtuzumab.\textsuperscript{19} Alemtuzumab is a humanized monoclonal antibody targeting the CD52 molecule, a glycoprotein present in high quantities in the membrane rafts of B-cells and T-cells, as well as other cells of the adaptive immune system. The role of the CD52 molecule is not known, but it may play a role in cell–cell interactions or T-cell migration and costimulation. Alemtuzumab mediates death of immune cells through cellular and complement-mediated induction of apoptosis, and the subsequent reconstitution of the immune system is characterized by changes in the number, proportions, and properties of the lymphocyte subsets. Namely, there is an increase in regulatory T-cells. T-regulatory cells mediate anergy and lessen T-cell responses; this response to alemtuzumab has been demonstrated both in patients and in vitro studies. Additionally, there is a change in the cytokine environment, a decrease in proinflammatory interleukin-gamma and interleukin (IL)-17, and an increase in anti-inflammatory IL-4, IL-10, and transforming growth factor-β. It is thought that this rebalancing of the immune system contributes to the therapeutic benefits, and results in persistent benefits long after clearance of the antibody.\textsuperscript{20–23}

The decrease in the level of circulating T and B lymphocytes occurs very rapidly, with the lowest values observed within days post-treatment. Lymphocytes repopulate over time, with B-cells returning first, usually with complete recovery within the year, and T-cell populations taking much longer.\textsuperscript{24}

The efficacy of alemtuzumab in MS is likely the result of multiple mechanisms of action. Administration of alemtuzumab results in depletion of circulating T and B lymphocytes within days. The sustained improvement in disability and brain atrophy, even in patients without clinically active disease, would suggest that the benefits seen with
Table 1 Drugs currently approved for treatment of multiple sclerosis in the USA and Europe

| Drug                                      | Year of approval | Route of administration and dosing | Mechanism of action                                                                 |
|-------------------------------------------|------------------|-------------------------------------|-------------------------------------------------------------------------------------|
| Interferon β-1b SC (Betaseron®)           | 1993             | 250 µg SC Every other day           | Downregulation of MHC class II and costimulatory molecules (CD80, CD40 on antigen-presenting cells; CD40L, CD28 found on T-cells); inhibits T-cell activation and promotes T-cell apoptosis.14 |
| Interferon β-1a IM (Avonex®)              | 1996             | 30 µg IM Once a week                | Same as Betaseron.                                                                   |
| Glatiramer acetate (Copaxone®)            | 1997             | 20 mg SC Daily                      | Four amino acid synthetic polymer based on the structure of myelin basic protein; attenuates regulatory T-cells, inhibits myelin-reactive T-cells. May be neuroprotective through stimulation of BDNF production. |
| Mitoxantrone (Novantrone®)                | 2000             | Usually 12 mg/m² Every 3 months up to a cumulative dose of 140 mg/m² | Antineoplastic drug. Acts through the suppression of T-cells, B-cells, and macrophages, thought to attack myelin.19 |
| Interferon β-1a SC (Rebi®)                | 2002             | 4 µg SC 3× per week                 | Same as Betaseron.                                                                   |
| Natalizumab (Tysabri®)                    | 2006             | 300 mg IV Every 4 weeks             | Monoclonal antibody against cell adhesion molecule α4-integrin, hampers movement of immune cells across the blood–brain barrier.19 |
| Fingolimod (Gilenya®)                     | 2010             | 0.5 mg orally, daily               | Spinosine-1-phosphate receptor modulator, retains lymphocytes in the lymph nodes, preventing entry to the CNS.19 |
| Teriflunomide (Aubagio®)                  | 2012             | 7 mg or 14 mg orally, daily        | Pyrimidine synthesis inhibitor that halts proliferation of T and B lymphocytes, inhibiting their function.19 |
| Dimethyl fumarate (Tecfidera®)            | 2013             | 120 mg 2× per day starter dose (1 week); 240 mg 2× per day thereafter | Exact mechanism unknown; thought to inhibit lymphocytes. Possible antioxidant function.19 |
| Alemtuzumab (Lemtrada®)                   | 2014             | IV infusion 5 on consecutive days, and then 3 consecutive days 1 year later | Anti-CD52 monoclonal antibody. Depletes B-cells, T-cells, monocytes, macrophages, and dendritic cells. Reconstitution results in different makeup of peripheral white blood cell counts.20,21 |

Abbreviations: BDNF, brain-derived neurotrophic factor; CNS, central nervous system; IV, intravenous; IM, intramuscular; SC, subcutaneous; MHC, major histocompatibility complex.

Alemtuzumab are not entirely anti-inflammatory, but also due to brain repair and neuroprotection promoted by an altered lymphocyte milieu.25,26 This includes the effects of an altered lymphocyte repertoire with a greater proportion of regulatory T-cells and secretion of neurotrophic factors. Studies have shown that when the reconstituted lymphocytes are stimulated with myelin basic protein, they secrete neurotrophic factors, including brain-derived neurotrophic growth factor, platelet-derived growth factor, and ciliary neurotrophic factor, which enhance neuronal repair, oligodendrocyte survival, and maturation and myelination.27

Another possible mechanism of action of alemtuzumab could come from its effect on the B-cell lymphocyte pool. Although initially postulated to be a T-cell-mediated autoimmune disease, increasing evidence points to involvement of B-cells as well.28 This evidence includes the presence of specific oligoclonal banding patterns in the cerebrospinal fluid of MS patients, demyelination in vitro with antibodies from MS patients,29 reported effectiveness of intravenous immunoglobulin therapy for treating a subset of MS patients,30–33 and the demonstrated efficacy of rituximab and ocrelizumab, which are anti-CD20, B-cell-depleting therapies in MS.29–34 Alemtuzumab produces profound and prolonged alteration in the reconstituted B-cell lymphocyte pool.35

Comparative efficacy, safety, and tolerability with respect to established treatments

There are currently ten treatments approved by the FDA for relapsing MS. The Phase III clinical trial data for newer agents including the oral medications and natalizumab and alemtuzumab are shown in Table 2.36–43

Alemtuzumab was initially tested in small open-label studies of MS patients in Cambridge, UK, beginning with 58 patients who had secondary progressive MS, followed by 22 patients who had failed other treatments.44 Results...
from these trials pointed to greater benefits in treating the early relapsing-remitting phase of the disease. After promising results from these early studies, alemtuzumab was tested in a Phase II study (CAMMS223) followed by two Phase III studies (CARE-MSI and CARE-MSII). In all three trials, alemtuzumab was compared with interferon β-1a subcutaneously (Table 3). In the Phase II CAMMS223 trial, 334 patients were randomized to receive subcutaneous interferon β-1a (44 μg three times per week) or annual infusions of alemtuzumab at two doses (12 mg or 24 mg per day). Inclusion criteria for this trial were previously untreated patients with disease duration of less than 3 years, an Expanded Disability Status Scale score of ≤3, a two or more clinical relapses in the preceding 2 years, and at least one gadolinium-enhancing lesion on monthly MRI scans obtained up to 4 months prior. Alemtuzumab treatment was suspended because three patients developed immune thrombocytopenic purpura, one of whom died; however, all but nine patients had received more than one infusion cycle (161 patients received two cycles; 45 patients received three). Treatment continued in the subcutaneous interferon β-1a arm. Alemtuzumab significantly reduced the rate of sustained accumulation of disability (9% versus 26.2%) and the annualized relapse rate (0.1 versus 0.36). The mean disability score improved by 0.39 in the alemtuzumab group and worsened in the interferon β-1a arm. On MRI analysis, the lesion burden was reduced, and brain volume was increased from baseline in the alemtuzumab group and reduced in the interferon β-1a group.

A 5-year extension study of participants in the Phase II trial of alemtuzumab continued to demonstrate long-term sustained benefits when compared with the interferon group. Over 5 years, alemtuzumab decreased the risk of sustained accumulation of disability by 72% and the relapse rate by 69% compared with interferon β-1a (P<0.0001). The annualized relapse rate from baseline to month 60 was 0.11 for

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**Table 2 Phase III trials**

| DMT Phase III trial | Duration | Patients (n) | Placebo/active comparator | ARR reduction versus placebo/active comparator | Reduced risk of disability progression |
|---------------------|----------|--------------|---------------------------|-----------------------------------------------|--------------------------------------|
| Natalizumab AFFIRM[48] | 2 years | Natalizumab, n=627 Placebo, n=315 | Placebo | 68% (P<0.001) | 42% (P<0.001) |
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Abbreviations: ARR, absolute risk reduction; BID, twice daily; DMT, disease-modifying therapy; GA, glatiramer acetate; IM, intramuscular; TID, three times daily; IFN, interferon; SC, subcutaneous.
Alemtuzumab and 0.35 for interferon β-1a. No new adverse safety events were noted during follow-up.46 The most recent long-term follow-up data published on alemtuzumab-treated patients in its clinical trials assesses efficacy and safety after a median of 7 years. A total of 87 patients participated in this observational study, including patients from CAMM223 and also those from the SM3 trial, where in addition to alemtuzumab, patients were also infused with an inert variant to prevent the development of antibodies to alemtuzumab.47 Fifty-two percent of patients in the 7-year follow-up required just two cycles of alemtuzumab. In the remaining patients, relapses resulted in three (36%), four (8%), or five (1%) cycles. The mean annualized relapse rate after alemtuzumab was 0.16 compared with 1.78 in the 2 years prior to treatment. A greater proportion of patients had a 6-month sustained reduction in disability than a sustained accumulation (43.5% versus 32.2%), and a similar trend was seen when the time period was increased to 12 months (37.7% versus 21.8%). Among the 87 patients, median disability improved following alemtuzumab, with 43 patients having “net improved” disability, 35 having “net worse”, and nine having “net unchanged”. A decrement in positive disability outcome was associated with older age and, to a lesser extent, longer disease duration at the time of treatment.48

Phase III studies compared alemtuzumab with interferon β-1a in treatment-naïve patients (CARE-MSI43) as well as in patients who had failed previous treatment (CARE-MSII43). In CARE-MS I, 581 patients were randomized in a 2:1 manner to receive alemtuzumab or interferon β-1a subcutaneously. Primary endpoints for this study were relapse rate and time to sustained accumulation of disability. Forty percent of interferon-treated patients and 22% of alemtuzumab-treated patients experienced a relapse, which corresponded to a 54.9% risk reduction (P<0.0001) in the alemtuzumab group. Eleven percent of interferon-treated patients and 8% of alemtuzumab-treated patients had disability progression; however, the difference between the groups did not reach statistical significance. On MRI parameters, including proportions of patients with gadolinium-enhancing lesions, new or enlarging T2 lesions, and brain volume loss, alemtuzumab

Table 3 Summary of Phase II and III trials of alemtuzumab in multiple sclerosis

| Study                  | CAMMS223a (Phase II)                  | CARE-MSI2 (Phase III)                  | CARE-MSII4 (Phase III)                  |
|------------------------|---------------------------------------|---------------------------------------|----------------------------------------|
| Study design           | Single-blind, randomized, active comparator | Single-blind, randomized, active comparator | Single-blind, randomized, active comparator |
| Length of study, months| 36                                    | 24                                    | 24                                     |
| Patients with RRMS treated | 222                                   | 376                                   | 426                                    |
| Annualized relapse rate, baseline | 1.3                                   | 1.8                                   | 1.7                                    |
| Endpoints              | Alem: 0.1                             | Alem: 0.18                            | Alem: 0.26                             |
|                        | IFN β-1a: 0.36                        | IFN β-1a: 0.39                        | IFN β-1a: 0.52                         |
| Relapse rate reduction | 74%                                   | 55%                                   | 49%                                    |
| Proportion relapse-free | 80% Alem versus 52% IFN β-1a          | 78% Alem versus 59% IFN β-1a          | 65% Alem versus 47% IFN β-1a           |
| Mean change in EDSS from baseline | Alem: −0.39                           | Alem: −0.14                           | Alem: −0.17                            |
| Proportion of patients with sustained disability progression | IFN β-1a: +0.38                      | IFN β-1a: −0.14                       | IFN β-1a: +0.24                        |
| Proportion of patients with freedom from clinical disability | Alem: 9%                               | IFN β-1a: 11%                         | IFN β-1a: 22%                          |
| MRI endpoints          |                                      |                                       |                                        |
| Proportion with gadolinium-enhancing T1 lesions at 24 months | Alem: 9%                              | IFN β-1a: 19%                         | IFN β-1a: 23%                          |
| Proportion of patients with new or enlarging T2 hyperintense lesions | IFN β-1a: 48%                         | IFN β-1a: 58%                         | IFN β-1a: 68%                          |
| Median change in volume of T2 hyperintense lesion | Alem: −16.4%                          | Alem: −9.3%                           | Alem: −1.3%                            |
| Other endpoints        |                                      |                                       |                                        |
| Median change in brain parenchymal fraction | Alem: −0.5%                           | Alem: −0.87%                          | Alem: −0.61%                           |
| Proportion of patients clinically and MRI disease-free | IFN β-1a: −1.8%                        | IFN β-1a: −1.49%                       | IFN β-1a: −0.81%                       |
|                        | IFN β-1a: 39%                         | IFN β-1a: 39%                         | IFN β-1a: 32%                          |
|                        | IFN β-1a: 27%                         | IFN β-1a: 27%                         | IFN β-1a: 14%                          |

Abbreviations: Alem, Alemtuzumab; ARR, absolute risk reduction; EDSS, Expanded Disability Status Scale; Alem, alemtuzumab; IFN, interferon; MRI, magnetic resonance imaging; RRMS, relapsing-remitting multiple sclerosis.
was superior to subcutaneous interferon β-1a. More patients in the alemtuzumab arm remained free from clinical disease activity and combined clinical and radiological disease. The CARE-MS II trial examined 667 patients with at least one relapse on interferon β or glatiramer, who were then randomized to alemtuzumab or subcutaneous interferon β-1a. The primary endpoints were relapse rate and time to sustained accumulation of disability. Fifty percent of the interferon group and 35% of the alemtuzumab group experienced a relapse, which corresponded to a 49.9% risk reduction in the alemtuzumab group and 20% in interferon-treated patients, and 13% of alemtuzumab-treated patients had disability progression, which corresponded to a 42% risk reduction; both of these differences were statistically significant. Alemtuzumab was superior to interferon for MRI parameters, including the proportion of patients with gadolinium-enhancing lesions, new or enlarging T2 lesions, and reduction in brain volume loss.

Safety and tolerability

The most common adverse events were infusion-associated reactions, which were seen in more than 90% of patients who received alemtuzumab. Most of these reactions were characterized by symptoms including fever, chills, myalgia, and rash, which are ameliorated largely by prior administration of antipyretics, antihistamines, and steroids. Serious infusion reactions occurred in 3%, including anaphylaxis in two patients.

Mild to moderate infections were seen more frequently in the alemtuzumab-treated group than in the interferon-treated group. There were more instances of herpes infections in the alemtuzumab group (16% versus 3% in the interferon group). These were predominantly oral infections and herpes zoster. Due to a high incidence of herpes infection in the days following infusion of alemtuzumab, the Phase III CARE MS II trial underwent a protocol amendment with addition of acyclovir prophylaxis during and in the early months following alemtuzumab infusion, with reduction in infection rate during this period. The rate of herpes infections decreased from 2.8% to 0.5% for the first course and from 2.1% to 0.4% for the second course of alemtuzumab. There were no deaths reported as a result of serious or opportunistic infections.

Secondary autoimmune disorders are a significant risk associated with use of alemtuzumab. Based on incidence in the clinical trials, the most common is thyroid disorder, including hyperthyroidism, hypothyroidism, and Graves’ disease, which occurred in 34% of patients.44 Immune thrombocytopenia was seen in 2% of patients treated with alemtuzumab in CAMMS223; the index patient who developed this condition in the clinical trial died from lack of recognition and failure to seek medical attention, ultimately succumbing to intracerebral hemorrhage.45 The subsequent cases were recognized early and appropriate intervention was taken, with favorable outcomes. Additionally, two patients developed anti-glomerular basement membrane disease (Goodpasture’s syndrome) and one patient developed membranous glomerulonephritis following treatment.46 There were rare (<0.2%) instances of neutropenia, hemolytic anemia, and pancytopenia. Forty-eight percent of patients in the 7-year follow-up analysis developed secondary autoimmunity, most of which had been reported in previous studies.47

In the clinical studies, 0.3% of alemtuzumab-treated patients developed thyroid cancer, compared with none in the interferon β-1a-treated group. In addition, two further cases of thyroid cancer were diagnosed in alemtuzumab-treated patients during observational studies. Melanoma was seen in 0.3% of patients treated with alemtuzumab. Rare cases of lymphoproliferative disorders and lymphoma, including mucosa-associated lymphoid tissue lymphoma, Castleman’s disease, and a case of non-Epstein-Barr virus-associated Burkitt’s lymphoma which was fatal following treatment have been reported in MS patients treated with alemtuzumab (http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM425409.pdf).

Patient-focused perspectives and profiles appropriate for alemtuzumab

There are one of two approaches one could adopt in treating MS, ie, induction versus escalation therapy. Induction or escalation of treatment could be achieved by using one highly efficacious agent or a simultaneous combination of therapies. Combination therapy has not been utilized to any significant extent in MS, likely because of the difficulties associated with administration of multiple injectables at the same time (as all the medications initially approved for MS were parenteral until the advent of fingolimod in 2010) and lack of data supporting increased efficacy from the combination of intramuscular interferon β-1a and glatiramer acetate in a large clinical trial.48

There is increasing knowledge that early optimal intervention provides the best opportunity to favorably influence the long-term outcome of MS. Suboptimal control of the disease early in its course might bring into play a cascade of
irreversible events that are not amenable to later treatment and would result in permanent disability. Given the importance of early effective treatment, one could use data from several studies that outline potential early prognostic indicators that might give us insight into an individual patient’s disease course when making appropriate treatment choices. For a patient who has unfavorable prognostic indicators, ie, multiple early relapses, severe relapses with residual deficits, significant brainstem/spinal cord involvement, or a large lesion burden on MRI, it might be prudent to use one of the more aggressive treatments as the patient’s first disease-modifying therapy or have a low threshold to switch to a more aggressive therapy at the earliest indication of a suboptimal response.

Generally, natalizumab appears to be more effective than the injectable treatments. Fingolimod was compared with intramuscular interferon β-1a in one of its Phase III trials and demonstrated greater efficacy. Dimethyl fumarate has not been compared in head-to-head trials with another agent, although one of its clinical trials included a glatiramer acetate arm. Alemtuzumab has demonstrated impressive efficacy when compared with subcutaneous interferon β-1a in three clinical trials. Based on the data we currently have, given its efficacy, it will be used for patients with highly active disease. As to its order of use in the treatment sequence, while in Europe the European Medicines Agency states that “Lemtrada is indicated for adult patients with relapsing remitting multiple sclerosis (RRMS) with active disease defined by clinical or imaging features” (http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003718/WC500150521.pdf), and hence it could be potentially used as first-line therapy, the FDA in its approval states that “Because of its safety profile, the use of Lemtrada should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.” Hence, in the USA, alemtuzumab will be used mainly as an escalation therapy rather than as an initial induction agent.

Despite its remarkable efficacy, because of the significant risk of secondary autoimmune disorders, prolonged immune suppression, potential risk of infections, and potential increased risk of certain malignancies, treatment with alemtuzumab should be undertaken only after a thorough risk versus benefit evaluation. The Risk Evaluation and Mitigation Strategy program mandated with use of alemtuzumab will serve to provide close vigilance for emergence of any adverse event and allow immediate remediation measures to lower the likelihood of a poor outcome. Patient adherence to this protocol has to be strictly enforced, and patient commitment to it ensured prior to initiation of treatment, and this will play an important role in patient selection.

Conclusion
Alemtuzumab is the newest medication in the armamentarium to treat MS. It has shown impressive long-term efficacy, and being administered as an infusion cycle once a year would pose no issues with treatment adherence. However, its use is associated with potentially serious adverse events, and the risks versus benefits would need to be carefully weighed for each patient before initiation of treatment. It is vital for patients to adhere to the long-term Risk Evaluation and Mitigation Strategy program and be closely monitored for any adverse event. Ultimately, its growth and expanding use in MS would depend on accumulation of positive patient and physician experience and with continued demonstration of sustained high efficacy over long-term safety concerns.

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Disclosure
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