National
Multiple Sclerosis
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News Sheets

MARKETING & DEVELOPMENT

March 21, 2013	**CC:** All
March 2013: E-communications Update	

March National MS eNEWS

Send date: 3/18/13
Audience: Full List

The March National MS eNEWS was sent on Monday, March 18. Content includes a feature about Society-funded research on dietary salt and MS, a report on the first meeting of the International Progressive MS Collaborative and a profile of Society Fellow Dr. Victoria Leavitt. Readers were also encouraged to participate in Walk MS events, to join MSConnection.org, and to donate as part of the Every Connection Counts campaign.

Contact Information

For editorial questions or suggestions regarding our National MS eNEWS, please contact Gary at gary.sullivan@nmss.org or 212-476-0538 (or 10538).

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National Multiple Sclerosis Society
News Sheets

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RESEARCH/CLINICAL UPDATE

March 21, 2013

Oxford's Professor George Ebers Wins 2013 John Dystel Prize for MS Research

Revolutionized our understanding of MS

Professor George C. Ebers, MD, of University of Oxford in London, has been chosen by a committee of his peers to receive the National MS Society/American Academy of Neurology's 2013 John Dystel Prize for Multiple Sclerosis Research. Dr. Ebers is being honored for his extensive contributions to understanding MS, shedding new light on factors such as genes that contribute to susceptibility to MS. The $15,000 prize is being presented this week at the annual meeting of the American Academy of Neurology in San Diego.

"Professor Ebers' achievements are unparalleled in the field, and he is still conducting research that is of the utmost relevance to understanding the disease," said Sreeram Ramagopalan, PhD (University of Oxford), a former student of Dr. Ebers, who nominated him for the prize.

Dr. Ebers' contributions:

Identifying the importance of genetic factors in MS: Dr. Ebers established the Canadian Collaborative Project on Genetic Susceptibility to MS in 1993, which has collected data on more than 30,000 people with MS and their families. In particular, his studies of twins have shown that susceptibility is partly genetic and partly environmental, indicating that MS is a complex genetic disease. These findings contribute to efforts to end MS through prevention. (**Proceedings of the National Academy of Sciences U S A** 2003;100:12877, http://www.ncbi.nlm.nih.gov/pubmed/14569025)

Dr. Ebers performed an early search for genes that make people susceptible to MS. This showed linkage to the Human leukocyte antigen (HLA) complex (genes related to the immune system) on chromosome 6. (**Lancet** 1982;2:88, http://www.ncbi.nlm.nih.gov/pubmed/6123820) Additional research has confirmed HLA as a key factor in genetic susceptibility to MS. More recent work by Dr. Ebers and others has highlighted the complexity of these genes' association with MS, with

some forms conferring increasing disease risk and some forms being protective. (**Proceedings of the National Academy of Sciences U S A** 2007;104:20896, http://www.ncbi.nlm.nih.gov/pubmed/18087043)

Dr. Ebers also has reported key findings on how genes interact with environmental factors. His team showed an association between a rare variation of a gene that controls vitamin D levels and the development of MS in rare families with multiple members who have the disease. This gene variation causes dysfunction that leads to vitamin D deficiency. Research is increasingly pointing to reduced levels of vitamin D in the blood as one factor that can increase the risk of developing MS. (**Annals of Neurology** 2011;70:881, http://www.ncbi.nlm.nih.gov/pubmed/22190362)

Delineating the natural history of MS: Dr. Ebers has performed detailed studies tracking over time the "natural history" of MS in London, Ontario, Canada, following more than 1,000 individuals since 1972. Natural history studies provide important knowledge, such as the average number of MS relapses a person may be expected to experience. This helps to appropriately design clinical trials and interpret their results. These studies have been published in a series of important papers on topics such as the predictive value of the early course of MS (**Brain** 1989;112:1419), and the features of primary progressive MS. (**Brain** 1999;122:625, http://www.ncbi.nlm.nih.gov/pubmed/10219776)

Epidemiology of MS: Dr. Ebers' studies have forged new paths our understanding of who gets MS, which is the goal of epidemiology. In a study of over 40,000 people from Canada, Sweden, Norway and the United Kingdom, Dr. Ebers showed that the relative risk of developing MS is higher if you are born in May and lower if you are born in November. The finding of a birth pattern suggests the possibility that the origins of the disease date to very early in life. (**British Medical Journal** 2005;330:120, http://www.ncbi.nlm.nih.gov/pubmed/15585537)

Dr. Ebers also has contributed to the study of gender differences in MS. Among other contributions, he documented in 2006 a significant increase in the number of women diagnosed with MS more than men, noting that the female to male ratio in the incidence of MS had increased progressively over the previous 50 years. (**Lancet Neurology** 2006;5:932, http://www.ncbi.nlm.nih.gov/pubmed/17052660)

A series of studies on the relatives of people with MS including spouses, half-siblings, adoptees, and step-siblings suggested the idea that increases in the risk for developing MS come less from the familial environment than from factors operating at a general population level, such as climate and/or diet. These studies led to examination of role of Vitamin D in MS risk and the potential of vitamin D supplementation for MS patients and their families. (**Lancet Neurology** 2008;7:268, http://www.ncbi.nlm.nih.gov/pubmed/18275928)

Sharing knowledge: Ebers has published extensively in the medical literature, with more than 300 publications in peer reviewed journals, three books, 25 book chapters, and multiple editorials. He

is listed in A & C Black's Who's Who (2012). Professor Ebers' career as a clinician-researcher was celebrated in June 2012 at a Festschrift at Corpus Christi College, University of Oxford, where researchers and clinicians from around the world met to pay tribute to his life's work.

About the Prize: The $15,000 Dystel Prize is given jointly by the National MS Society and the American Academy of Neurology, and is funded through the Society's John Dystel Multiple Sclerosis Research Fund. Society Honorary Life National Board of Directors member Oscar Dystel and his late wife Marion established this fund in 1994 in honor of their son John Jay Dystel, an attorney whose promising career was cut short by progressive disability from MS. (John died of complications of the disease in June 2003.) Previous winners of the Prize are Drs. Donald Paty (1995), Cedric Raine (1996), John Kurtzke (1997), Henry McFarland (1998), W. Ian McDonald (1999), Kenneth Johnson (2000), John Prineas (2001), Stephen Waxman (2002), Bruce Trapp (2003), Lawrence Steinman (2004), Jack Antel (2005), William Sibley (2006), Howard Weiner (2007), Stephen Hauser (2008), David Miller (2009), David Hafler (2010), Brian Weinshenker (2011), and Richard Ransohoff (2012). Read more (http://www.nationalmssociety.org/for-professionals/researchers/get-funding/john-dystel-prize/index.aspx) about other Dystel Prize winners.

Biography: George Cornell Ebers, MD, is Action Research Professor of Clinical Neurology and Adjunct Professor, in the Department of Clinical Neurological Sciences at the University of Oxford. Dr. Ebers received his medical degree from the University of Toronto and completed an internship at Royal Victoria Hospital in Montreal. He practiced briefly in family medicine, and then completed a residency in Neurology at Cornell Medical Center in New York, ending his term there as Chief Resident and Instructor in Neurology. Before moving to Oxford in 1999, Dr. Ebers practiced at the London Health Sciences Centre in Ontario, where he was a professor in the Department of Clinical Neurological Sciences, with cross-appointments in the Departments of Medicine, Microbiology and Immunology, and Biochemistry at the University of Western Ontario. Among the many awards given to Ebers are the Wainright Scholarship; JB Colling Prize in Medicine; Recipient Research Career Development Award; MS Society of Canada Ministry of Health Career Scientist Award; Pringle Medal; and the University of Western Ontario Faculty of Medicine Award of Excellence.

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RESEARCH/CLINICAL UPDATE

March 27, 2013

FDA Approves Twice a Day Capsules Called Tecfidera™ (formerly called BG-12) for Relapsing MS

The U.S. Food and Drug Administration has approved Tecfidera™ capsules (dimethyl fumarate, Biogen Idec –formerly "BG-12") as a first-line disease-modifying therapy for people with relapsing forms of MS (http://www.nationalmssociety.org/about-multiple-sclerosis/relapsing-ms/index.aspx). This makes the third oral therapy approved for relapsing MS, and the tenth disease-modifying treatment available in the U.S. Tecfidera is expected to be available by prescription within a few days.

"The approval of Tecfidera is an important expansion of therapeutic options, and increases our ability to find effective and tolerable treatment solutions for individual patients," said Bruce A. Cohen, MD, Professor, Davee Department of Neurology and Clinical Neurosciences at Northwestern University's Feinberg School of Medicine, and Chair of the National MS Society's National Medical Advisory Committee. "As with all newly-approved treatments, we will learn more about the benefits and safety of Tecfidera over time," he added.

"The approval of Tecfidera is encouraging news for people who have relapsing forms of MS," noted Timothy Coetzee, PhD, Chief Research Officer at the National MS Society. "Having ten disease-modifying therapies available for relapsing forms of MS further motivates us to gather the forces of the global community to make similar strides for people with progressive forms of MS, for whom there are fewer options." Read more about the International Progressive MS Collaborative (http://www.nationalmssociety.org/news/news-detail/download.aspx?id=45592)

Read the FDA's press release
(http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm345528.htm)

About Tecfidera: Multiple sclerosis involves immune system attacks against brain and spinal cord tissues. Although its exact mechanism of action is not known, Tecfidera is thought to inhibit immune cells and molecules, and may have anti-oxidant properties that could be protective against damage to the brain and spinal cord. A chemically related compound, called Fumaderm (dimethyl fumarate and fumeric acid esters), has been used for decades in Germany to treat acute flare-ups of psoriasis. Tecfidera is a new, different formulation of dimethyl fumerate that was developed by Biogen Idec specifically for the treatment of multiple sclerosis.

Potential benefits: Twice-daily Tecfidera was shown in clinical trials to significantly reduce relapses and disease activity on MRIs, and in one trial it reduced progression of disability. The FDA's approval was based largely on results of two large-scale phase III studies of Tecfidera capsules, called DEFINE and CONFIRM, which were conducted in people with relapsing-remitting MS. The results were published in 2012. Read a summary (http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6906)

In the DEFINE trial, there was a significant reduction in the proportion of people on Tecfidera who experienced relapses at 2 years, compared with those on inactive placebo. For those on the approved twice-daily dose, 27% experienced relapses, versus 46% of those on placebo -- a 49% reduction in the risk of relapse. All secondary outcomes were also met in the Tecfidera groups, including significant impact on disease activity detected with MRI, and reduction in the risk of confirmed progression of disability (detected by the EDSS, a standard scale that measures disability). The proportion of those who progressed over two years was 16% for twice-daily Tecfidera versus 27% for placebo – a 38% reduction in the risk of disability.

In the CONFIRM trial, there was a significant reduction in the average annual number of MS relapses (annualized relapse rate, or ARR) in the Tecfidera groups versus placebo. For those on the approved twice-daily dose, ARR was reduced by 44% versus placebo. Results in secondary endpoints included significant reductions in disease activity on MRI and the proportion of patients experiencing relapses in the Tecfidera groups versus placebo. Disability progression was not reduced significantly in the Tecfidera groups compared to the placebo group.

Potential risks and screenings: The most common adverse events experienced by people taking Tecfidera during the trials were flushing (which can create a sensation of heat or itching and a red blush on the skin) and gastrointestinal events (such as diarrhea, nausea, and upper abdominal pain). During the clinical trials, up to 40% of participants experienced flushing, and some experienced gastrointestinal events. The incidence of these events was highest in the first month of treatment, decreasing thereafter. Tecfidera reduced blood lymphocyte (white blood cell) counts but no significant or severe infections were reported. Liver enzyme tests were elevated, but there were no reports of significant liver injury or liver failure.

Before starting treatment, the FDA recommends that a person's health care provider assess a recent (within 6 months) blood cell count, and repeat the blood cell count annually thereafter.

Before starting treatment with Tecfidera, women should talk to their health care providers if they are pregnant or planning to become pregnant.
Taking a disease-modifying therapy is currently the best way to reduce MS disease activity and future deterioration. Selecting an MS therapy should be done by people with MS in collaboration with their MS doctors, taking into account a variety of factors, including the effectiveness of any therapy they are currently using, and weighing potential risks and benefits, costs and lifestyle factors.

For more information about support services provided by Biogen Idec, people can contact the company's MS *ActiveSource*® Program. MS *ActiveSource* is available by phone at 1-800-456-2255 or on the Web at www.MSActiveSource.com.

Download the Prescribing Information (.pdf) http://www.tecfidera.com/pdfs/full-prescribing-information.pdf

Read more about disease-modifying therapies and other treatments for MS and MS symptoms:
http://nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/treatments/index.aspx
Read about National MS Society efforts to speed research in progressive MS:
http://nationalmssociety.org/research/research-we-fund/research-in-progressive-ms/index.aspx

FAQ About FDA's Approval of Oral Dimethyl Fumarate – Brand name Tecfidera™ – for Relapsing MS

Q. What is Tecfidera?
A. Tecfidera is an oral therapy contained in capsules taken two times per day. Tecfidera, formerly known as BG-12, is dimethyl fumerate, a formulation that was developed specifically for use by people with multiple sclerosis. A chemically related compound, called Fumaderm (dimethyl fumarate and fumeric acid esters), has been used at higher doses for decades in Germany to treat acute flare-ups of psoriasis. Although its exact mechanism of action is not known, Tecfidera is thought to inhibit immune cells and molecules, and may have anti-oxidant properties that could be protective against damage to the brain and spinal cord.

Q. What types of MS is Tecfidera approved to treat?
A. The FDA has approved Tecfidera for the treatment of patients with relapsing forms of MS (http://www.nationalmssociety.org/about-multiple-sclerosis/relapsing-ms/index.aspx). In other words, people who experience periodic MS attacks, such as those who have relapsing-remitting MS or secondary-progressive MS with relapses.

Q. How is Tecfidera taken?
A. The capsules are taken orally twice per day. When Tecfidera is begun, individuals will be provided with a one-week reduced starter dose, and thereafter a maintenance dose, both taken twice daily.

Q. When will Tecfidera be available by prescription?
A. Tecfidera is expected to be available by prescription within a few days.

Q. How effective is Tecfidera?
A. In phase III clinical trials of Tecfidera capsules (http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6906), Tecfidera significantly reduced the proportion of people who experienced relapses at 2 years, compared with those on placebo. Those on the twice-daily dose had a 49% reduction in the risk of relapse compared to those on placebo. Tecfidera also reduced the average annual number of relapses (annualized relapse rate) by 44% compared to placebo. The therapy also had a significant impact on disease activity detected with MRI. In one of two phase III trials, Tecfidera also reduced the risk of confirmed progression of disability (detected by the EDSS, a standard scale that measures disability). The proportion of those who progressed over two years was 16% for twice-daily Tecfidera versus 27% for placebo – a 38% reduction in risk of disability.

Q. What are the potential side effects of Tecfidera?
A. Tecfidera may cause flushing (which can create a sensation of heat or itching and a red blush on the skin) and gastrointestinal events (such as diarrhea, nausea, and upper abdominal pain). The incidence of these events during clinical trials was highest in the first month of treatment, decreasing thereafter. Taking Tecfidera with food may reduce flushing. Tecfidera reduced blood lymphocyte (white blood cell) counts but no significant or severe infections were reported. The Prescribing Information (http://www.tecfidera.com/pdfs/full-prescribing-information.pdf) provides full information on potential side effects.

Q. Why should a person with MS consider taking a disease-modifying therapy?
A. Taking a disease-modifying therapy is currently the best way to reduce MS disease activity and future deterioration. Studies comparing people in clinical trials who started therapy earlier than those on inactive placebo suggest that early treatment offered important benefits against the accumulation of disability, which were generally not experienced to the same degree by those who started treatment later..

Selecting an MS therapy should be done by people with MS in collaboration with their MS doctors, taking into account a variety of factors, including the effectiveness of any therapy they are currently using, and weighing potential risks and benefits, costs and lifestyle factors.

Q. Should I switch from my current therapy to Tecfidera?

A. The decision about whether to take Tecfidera should be made in collaboration with your MS doctor, taking into account a variety of factors including the effectiveness of any therapy you are currently using, the potential risks and benefits, as well as costs and lifestyle factors. Important questions to be considered and discussed with your doctor in terms of Tecfidera include:

- How am I doing on my current therapy?
- What is my tolerance for the risk of known side effects?
- What is my tolerance for the risk of adverse consequences that might emerge with longer-term use?
- How will my medication choice affect my ability or plans to become pregnant?
- What are the comparative costs of my current therapy versus Tecfidera?

Q. How does the effectiveness of Tecfidera compare to other available therapies?
A. Tecfidera has not been compared in head-to-head trials to other available therapies. Although one group during the CONFIRM clinical trial was receiving glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries) as a reference, the study was not designed to compare the effectiveness of Tecfidera versus Copaxone.

Q. How long would a person take Tecfidera?
A. There is no specified time limit for taking Tecfidera.

Q. Are there any risk factors or medical conditions that would make it inappropriate for an individual to take Tecfidera?
A. The prescribing information does not list factors that would make taking Tecfidera inappropriate, but health care providers should consider withholding treatment in those with serious infections until those infections resolve.

Tecfidera is rated as a Pregancy Category C. There have been no adequate studies in pregnant women, but based on animal studies, Tecfidera may cause harm to the fetus.

Q. Will a person taking Tecfidera have to get any special medical tests or monitoring?
A. Before people begin taking Tecfidera, their health care providers should assess a recent (within 6 months) blood cell count. Thereafter, the FDA recommends annual blood counts and as clinically indicated. Health care providers should consider withholding treatment in those with serious infections until those infections resolve.

Q. What will Tecfidera cost?
A. The price has not been announced, but the actual cost to an individual who has MS will depend on the provisions of his or her insurance coverage and the degree to which that individual will be eligible for programs designed to assist with out-of-pocket costs.

Q. Will my health insurance cover Tecfidera?
A. Coverage will depend on individual insurance plans.

Q. Is there a generic form of Tecfidera?
A. No.

Q. Where can I get information about the patient support that Biogen Idec plans to provide?
A. For more information about support services provided by Biogen Idec, people can contact the company's MS *ActiveSource*® Program. MS *ActiveSource* is available by phone at 1-800-456-2255 or on the Web at www.MSActiveSource.com.

Q. Are there other oral disease-modifying therapies available or in development for MS?
A. Yes, there are other oral therapies available now or in development. Gilenya® (http://nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/treatments/medications/fingolimod/index.aspx) and Aubagio® (http://www.nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/treatments/medications/aubagio/index.aspx) are oral disease-modifying therapies approved for relapsing forms of MS. An oral therapy in later stages of development for relapsing MS is laquinimod (sponsored by Teva Pharmaceutical Industries). Read more about ongoing clinical trials in MS: http://nationalmssociety.org/research/clinical-trials/clinical-trials-in-ms/index.aspx

Q. I've been hearing news about other new treatments in development for MS. What are some details?
A. Genzyme has applied for FDA approval of the experimental therapy alemtuzumab, given by a cycle of IV infusions once per year, to treat relapsing MS, based on positive results from several clinical trials. An FDA decision is expected by the end of 2013. Oral and infrequent-dose disease-modifying therapies are just two of many exciting research avenues that address ways to stop MS progression, restore function and end MS forever. Just a few new approaches being explored include potential benefits of the hormone estriol, adult stem cell transplantation, large-scale clinical trials for progressive MS, trials of agents aimed at protecting the nervous system, and studies of vitamin D and CCSVI (chronic cerebrospinal venous insufficiency – http://www.nationalMSsociety.org/ccsvi). In addition, the newly formed International Collaborative on Progressive MS (http://www.nationalmssociety.org/news/news-detail/download.aspx?id=45592) is a global effort to speed research and treatments on progressive MS.

Q. Is Tecfidera being tested in progressive MS?
A. Not at this time.

Q. Why aren't there more treatments for progressive MS?
A. Nearly every therapy approved for relapsing MS has been tested, or is now in testing, in people with progressive forms of the disease, including primary-progressive MS and secondary-progressive MS. Up to now, clinical trials involving people with relapsing MS often rely on

counting relapses or doing MRI scans to detect immune activity. The fact that there is no easy way to detect progression quickly is one reason why development of therapies for progressive MS is behind. The National MS Society is investing in better ways to detect benefits of therapies for progressive forms of MS. Right now there are large clinical trials going on in progressive MS, including tests of Tysabri,® Gilenya,® Ocrelizumab, and Masitinib. Download a table of trials on focusing on progressive MS (.pdf): http://nationalmssociety.org/research/clinical-trials/clinical-trials-in-ms/download.aspx?id=41747