AD Vaccine Shows Promise

Though preliminary, a new study published online June 6 in *Lancet Neurology* is reporting positive effects of an active vaccine against Alzheimer’s disease. The new vaccine, CAD106, involves active immunization, using a type of vaccine designed to trigger the body’s immune defense against beta-amyloid. In this second clinical trial on humans, the vaccine was modified to affect only the harmful beta-amyloid. Researchers report that 80 percent of the patients involved in the trials developed their own protective antibodies against beta-amyloid without suffering any side effects over the three years of the study. The researchers believe this suggests that the CAD106 vaccine is a tolerable treatment for patients with mild to moderate Alzheimer’s.

The researchers carried out a Phase I, double-blind, placebo-controlled, 52-week study in two centers in Sweden. Participants, 50 to 80 years old, with mild-to-moderate AD, were placed into one of two groups according to time of study entry. They were then randomly allocated to receive either CAD106 or placebo (4:1; group one received CAD106 50μg or placebo, group two received CAD106 150μg or placebo). Each patient received three subcutaneous injections. “All patients, caregivers, and investigators were masked to treatment allocation throughout the study. Primary objectives were to assess the safety and tolerability of CAD106 and to identify the Aβ-specific antibody response,” the researchers write. They assessed safety by recording all adverse events, MRI scans, physical and neurological examinations, vital signs, electrocardiography, electroencephalography, and laboratory analysis of blood and CSF. Patients with Aβ-IgG serum titres higher than 16 units at least once during the study were labeled as responders.

Between August 2005 and March 2007, the authors randomly allocated 31 patients into cohort one (24 patients to CAD106 treatment and seven to placebo) and 27 patients into cohort two (22 patients to CAD106 treatment and five to placebo). Fifty-six of 58 patients reported adverse events. In cohort one, nasopharyngitis was the most commonly reported adverse event (10 of 24 CAD106-treated patients). In cohort two, injection site erythema was the most commonly reported adverse event (14 of 22 CAD106-treated patients). “Overall, nine patients reported serious adverse events—none was thought to be related to the study drug. We recorded no clinical or subclinical cases of meningoencephalitis.” Sixteen of 24 (67 percent) CAD106-treated patients in cohort one and 18 of 22 (82 percent) in cohort two developed Aβ antibody response meeting pre-specified responder threshold. One of 12 placebo-treated patients (eight percent) had Aβ-IgG concentrations that qualified them as a responder.

“This paper is very important so far,” says Ronald Devere, MD, who was not part of the study and is Director of the Taste and Smell Disorders Clinic and Alzheimer Disease & Memory Disorders Center in Austin, TX. “The vaccine for Alzheimer’s that was used in a human trial a number of years ago was taken off the testing market because it induced encephalitis in five or six patients, which is a very serious side effect,” Dr. Devere added. This was due to T-cells attacking the brain in some cases.

In those patients who received the older vaccine and who didn’t get encephalitis but died otherwise, their brains showed removal of Amyloid even though clinically they didn’t get better, Dr. Devere said. “The thinking at the time was if a safe vaccine was developed and given earlier in Alzheimer’s disease or even in those with MCI or presymptomatic Alzheimer’s that would be potentially a major breakthrough in treatment if successful. This current study so far has suggested this goal by not causing serious side effects, especially encephalitis, and getting a good antibody response using two different doses of the vaccine.”

Dr. Devere believes the next step is to expand the vaccine to more patients and controls, and follow those already vaccinated to see if dementia improves or stabilizes. If it’s found to be safe in the patients with AD and demonstrates less amyloid present in the brain, Dr. Devere believes researchers can use it in MCI cases, as well as normal subjects who have significant amyloid in the brain. It could also have value for other tests to suggest the probability of future Alzheimer’s. “In this way amyloid can be removed very early in those at-risk and may prevent the disease expressing itself later on,” he says. “This is all exciting and promising, but we must not get overly excited yet.”

The study was carried out by Professor Bengt Winblad at Karolinska Institute’s Alzheimer’s Disease Research Centre in Huddinge. This study is registered with ClinicalTrials.gov, number NCT00411580.
TOWER Power: Positive Top Line MS Data

Encouraging top-line data from a Phase III trial demonstrated that patients with relapsing forms of multiple sclerosis who received Aubagio (teriflunomide, Sanofi) showed significant reductions in annualized relapse rates. The results are from the TOWER trial, which was conducted on 1,169 patients and evaluated Aubagio in two dosage strengths: 7mg and 14mg. Patients in the 14mg dosage arm displayed a 36.3 percent decrease in annualized relapse rate compared to placebo. Additionally, a 31.5 percent decrease in the risk of 12-week sustained accumulation of disability was also observed.

Regulatory submissions for Aubagio are currently under review, with FDA anticipated to make a decision this summer and the European Medicines Agency scheduled to provide feedback at the start of 2013. The company indicated that full data from the study will be presented at a future medical meeting.

Potiga Tablets, CV Now Available

Potiga Tablets, CV (ezogabine, GlaxoSmithKline) are now available as adjunctive treatment of partial-onset seizures in patients aged 18 years and older. Availability follows the decision of the DEA to classify the product as schedule V of the Controlled Substances Act, allowing Potiga to be made available to physicians to prescribe for appropriate patients. The FDA approved Potiga in June 2011, as the first potassium channel opener indicated for adjunctive treatment of partial-onset seizures in adults.

Alzheimer’s Drug Meets Primary Endpoint

Patients receiving the investigational compound Lu AES8054 achieved statistically significant improvement in cognitive performance when added to Aricept (donepezil), according to developer Lundbeck. The compound is a novel, selective SHT6 receptor antagonist with a different mechanism of action than currently available Alzheimer’s medications.

Augmentation therapy with Lu AES8054 (plus 10mg/day donepezil) at the selected dose resulted in statistically significant improvement in cognition, as measured by the ADAS-cog (Alzheimer’s Disease Assessment Scale-cognitive sub-scale) over a 24-week treatment period versus placebo (plus 10mg/day donepezil). Secondary endpoints, including measures of global status and activities of daily living, also showed positive trends with the addition of Lu AES8054, compared with patients who only received donepezil, according to the company. The drug was well tolerated.

Horizant Approved for PHN

FDA approved Horizant (gabapentin enacarbil) Extended-Release Tablets for the management of postherpetic neuralgia (PHN) in adults. The recommended dose for the management of PHN in adults is 600mg twice daily. Treatment should be initiated at a dose of 600mg in the morning for three days followed by 600mg twice daily (1,200 mg/day) beginning on day four. Doses must be adjusted in patients with impaired renal function. In a 12-week, controlled study in patients with PHN, somnolence and dizziness were the most frequently reported side effects. Somnolence was reported in 10 percent of patients treated with 1,200mg of Horizant per day compared with eight percent of patients receiving placebo. Dizziness was reported in 17% of patients receiving 1,200mg of Horizant per day compared with 15 percent of patients receiving placebo.

Lemtrada Submitted to FDA, EMA for Relapsing MS

Genzyme, a Sanofi company, has submitted a supplemental Biologics License Application (sBLA) to the FDA and a marketing authorization application (MAA) to the European Medicines Agency (EMA) seeking approval of Lemtrada (alemtuzumab) for treatment of relapsing multiple sclerosis. In two Phase III studies, results for Lemtrada were superior to high-dose subcutaneous interferon beta-1a on clinical and imaging endpoints, including a reduction in relapse rate. Genzyme is developing Lemtrada in MS in collaboration with Bayer HealthCare. See AAN Meeting updates (p. 12) for more coverage of alemtuzumab data.

NAAMA Convention in July

The National Arab-American Medical Association 26th International Medical Convention is July 7-12 in Istanbul, Turkey. Details and registration online: www.naama.com or call (248) 646-3661.
Soy-vey! Soy Supplements Don’t Help Thinking Skills

Soy supplements taken daily won’t improve the overall thinking abilities of your older female patients, according to a new study published June 5 in *Neurology*.

“There was no significant between-group difference on change from baseline in global cognition (mean standardized improvement of 0.42 in the isoflavone group and 0.31 in the placebo group; mean standardized difference 0.11, 95% confidence interval [CI] −0.13 to 0.35),” the authors write. Secondary analyses indicated superior improvement on a visual memory factor in the isoflavone group (mean standardized difference 0.33, 95% CI 0.06–0.60) “but no significant between-group differences on three other cognitive factors or individual test scores, and no significant difference within a subgroup of younger postmenopausal women.”

A total of 350 healthy postmenopausal women aged 45–92 years enrolled in the trial; 313 women with baseline and endpoint cognitive test data were included in intention-to-treat analyses. Adherence in both groups was nearly 90%.

Tysabri Risks Quantified

A quantitative risk stratification algorithm developed by Biogen Idec and Elan is intended to help physicians and people with MS have more confidence in considering Tysabri therapy, the companies say. Research published in the *New England Journal of Medicine* in May used data from clinical studies, post-marketing sources, and an independent Swedish registry to estimate the incidence of PML among Tysabri-treated patients. Data from 212 confirmed cases of PML among 99,571 Tysabri-treated patients were used to develop the risk stratification algorithm based on three established risk factors for PML: anti-JCV antibody status, prior use of immunosuppressant (IS) therapy, and duration of treatment with Tysabri (one to 24 months vs. 25 to 48 months).

The risk of PML increased with longer duration of Tysabri treatment, with the greatest increase observed after two years of therapy. Data beyond four years of therapy were limited.

Prior IS use was more common in patients who developed PML (34.5 percent) compared to patients in the global TYGRIS study (20.3 percent), indicating that prior IS use was associated with an increased risk of PML. The prevalence of anti-JCV antibodies in the general MS population was 54.9 percent and differed from the 100 percent anti-JCV antibody positivity observed in the 54 MS patients who developed PML and had known pre-PML anti-JCV antibody status. Because all 54 MS patients with known pre-PML anti-JCV antibody status tested positive, a sensitivity analysis assuming one hypothetical anti-JCV antibody negative PML patient was used to estimate the PML risk in antibody negative patients.

The Tysabri US label and EU Summary of Product Characteristics were updated to add anti-JCV antibody status as a risk factor for PML. The STRATIFY JCV assay is now available; it is the first blood test to be market authorized for the qualitative detection of antibodies to the polyomavirus JC virus.

Forget the Sugar

A study on rats published in the *Journal of Physiology* suggests that fructose slows down the brain and memory functions. It also demonstrated omega-3 fatty acids helped negate the effect. “Our findings illustrate that what you eat affects how you think,” said Fernando Gomez-Pinilla, a professor of neurosurgery at the David Geffen School of Medicine at UCLA and a professor of integrative biology and physiology in the UCLA College of Letters and Science, in an interview with *National Geographic*. “Eating a high-fructose diet over the long term alters your brain’s ability to learn and remember information. But adding omega-3 fatty acids to your meals can help minimize the damage.”

For the study, Gomez-Pinilla and his team examined two groups of rats. Both groups were administered drinking water spiked with fructose solution, but the second group was also fed flaxseed oil and docosahexaenoic acid (DHA), which contain omega-3 fatty. “The second group of rats navigated the maze much faster than the rats that did not receive omega-3 fatty acids,” Dr. Gomez-Pinilla said. “The DHA-deprived animals were slower, and their brains showed a decline in synaptic activity. Their brain cells had trouble signaling each other, disrupting the rats’ ability to think clearly and recall the route they’d learned six weeks earlier.”

New Merz CEO Eyes Growth in Neurology

William “Bill” Humphries, newly appointed CEO of Merz, Inc., has been spending some time “learning and listening.” When he spoke with *Practical Neurology* just a few days after assuming his new post, Mr. Humphries said that was his main task when he first came onboard—an important first step for a company currently undergoing a comprehensive business review.

The review is intended to assure appropriate protocols within the company and hopefully speed resolution of an injunction.
that bars the marketing of Xeomin (incobotulinumtoxinA) for aesthetic indications in the US and impacts marketing of Xeomin for therapeutic indications in discreet areas of the country.

On March 12, just days before Xeomin for Aesthetic use was to launch, Allergan issued a release detailing an injunction against Merz. For its part, Merz was somewhat quiet, offering limited though optimistic comments about the status of Xeomin. And then the company emerged with its own news: Bill Humphries, a veteran of the dermatology pharmaceutical industry was taking the helm as CEO of Merz, Inc., the US subsidiary of the privately-held German-based Merz Pharma Group. Mr. Humphries assumed overall responsibility for the Medical Dermatology global business unit and will oversee strategic direction and collaboration among three North American companies: Merz Pharmaceuticals, LLC, Merz Aesthetics, Inc. and Merz Pharma Canada, Ltd.

Characterizing the injunction as an “interruption,” Mr. Humphries now is focused on the future and moving Merz forward.

In addition to learning and listening, Mr. Humphries has done a good deal of setting the record straight. The “impact of the injunction isn’t dramatic,” he insists. As a private company with more than 100 years in business, Merz didn’t face any potential stock devaluation with the recent litigation. While Xeomin for aesthetic indications is expected to be a superstar in Merz’s portfolio, multiple successful agents continue to do well, Mr. Humphries points out. These include Radiesse, Asclera, Mederma—which he calls “a great franchise”—and its therapeutic agents, including Naftin and Xeomin therapeutic. In fact, Naftin accounts for 30 percent of the company’s current revenue.

Merz isn’t 10 months from bankruptcy, either. Although some reports quoted Merz representatives as saying the injunction would essentially shutter the business in less than a year, Mr. Humphries says certain comments were repeated out of context. During a pleading, a lawyer for Merz attempted to underscore the potential severe impact of harsh penalties against the company by suggesting a detrimental blow to the company’s financials, but that was a worst case scenario and not reflective of the current situation, Mr. Humphries assures.

There is no grand animosity between the toxin marketers. Of his former colleagues at Allergan, Mr. Humphries characterizes recent interactions as, “very collegial…We’ve moved past it.”

As it moves forward, Merz is focused on growing its presence in dermatology and in neurology. “We’ve got a great sales force out there, and we want to build this to be a big player in neurology,” Mr. Humphries says.

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**Annual Meeting Research Briefs**

**Study Shows Benefits of Early Lacosamide Add-On Therapy**

Interim results from the VITOB™ (VImpa™ added to One Baseline AED) study, presented at the AAN Annual Meeting, show that certain patients (those with less refractory partial-onset seizures) treated with Vimpat (lacosamide) C-V as add-on to monotherapy experienced seizure reduction. The interim analysis included efficacy data for 99 patients and safety data for 109 patients in a six-month prospective, non-interventional study of the efficacy, safety and tolerability of lacosamide when added to a single AED in patients with partial-onset seizures.

The majority of patients (73.4 percent) in the study had received only one to three AEDs since diagnosis. The mean lacosamide maintenance dose was 250mg/day and the median dose was 200 mg/day.

The greatest benefit was seen among patients treated with only one lifetime AED prior to adding-on lacosamide. Compared to the overall study population, one-AED patients experienced the greatest benefit from add-on therapy with lacosamide, with 86.7 percent showing a 50 percent or greater reduction in seizure frequency (vs. 77.8 percent of the overall study population) and 80 percent showing a more than 75 percent or greater reduction in seizure frequency (vs. 64.6 percent of the overall study population). Of note, 66.7 percent of those with a history of one lifetime AED experienced seizure freedom (vs. 43.4 percent of the overall study population).

The current data, though preliminary, “does reflect real-world patient population and treatment settings,” observes Kelly Simontacchi, PhD, Medical Director for CNS at UCB. “The findings support Vimpat’s efficacy in patients who have failed monotherapy with another agent.”

Given that patients with one previous AED exposure had better response than those receiving two or more AEDs, the findings thus far seem to suggest that clinicians should consider adjunctive therapy sooner than later, Dr. Simontacchi says. “It seems that clinicians should look to add-on therapy earlier in the treatment algorithm when partial onset seizure patients have less lifetime AED exposure. Of course, these results need to be confirmed when the study ends,” she says.

Treatment emergent adverse events (TEAEs) included...
Fatigue (11.9%), dizziness (10.1%) and convulsion (5.5%). The overall rate of reported AEs (50.5 percent) was lower than that seen in the pivotal trials for lacosamide (81 percent for all doses). Vimpat is indicated as an adjunctive therapy for the treatment of partial-onset seizures in adults with epilepsy.

Data Demonstrate Benefits of Rotigotine Transdermal System for RLS, Non-motor Symptoms of PD

Just weeks after FDA approved Neupro® (rotigotine transdermal system, UCB, Inc.) for the treatment of the signs and symptoms of advanced stage idiopathic Parkinson’s disease (PD) and as a treatment for moderate-to-severe primary Restless Legs Syndrome (RLS), data presented at the AAN Annual meeting demonstrated the efficacy of the agent for each indication and early stage idiopathic PD for which Neupro was previously approved.

Post-hoc analyses of pivotal clinical trials of Neupro in patients with RLS/Willis Ekbom disease found improvements with rotigotine versus placebo in most of the single items from the International RLS Study Group Rating Scale (IRLS). The post-hoc analyses were based on data from the two phase III, double-blind, six-month placebo-controlled trials that investigated the effect of rotigotine on specific features of RLS by examining single item scores from IRLS related to core RLS symptoms (sensory-motor dysfunction), degree of severity (days and hours within day with symptom), and symptom impact on sleep, mood and daily life.

In the European study rotigotine was shown to provide improvements versus placebo in nine of 10 individual IRLS items: Discomfort in legs or arms, Need to move around, Severity of RLS as a whole, Average severity when symptoms occurred, Frequency of symptoms, Severity of sleep disturbance, Tiredness or sleepiness during the day, Impact on ability to carry out daily affairs, and Severity of mood disturbance. In the US study, rotigotine was shown to provide improvements versus placebo in all of the same items except for severity of mood disturbance. Unlike in the European study, rotigotine was associated with improvement in relief of RLS discomfort by movement.

According to Richard Allen, PhD, Research Associate in the Department of Neurology at Johns Hopkins University in Baltimore, the positive findings for rotigotine suggest exciting directions for the management of RLS. While dopaminergic agents have been useful for the management of RLS symptoms, these short-acting agents have left patients vulnerable to worsening of RLS symptoms as the drugs wear off. Furthermore, these agents are shown to modify the body’s dopamine system, Dr. Allen points out. By contrast, rotigotine patch is longer-acting, reducing the likelihood of wearing-off. Patients may experience more consistent symptom relief with rotigotine, he suggests. Plus, he points out, the agonist does not modify the function of the dopamine system and may therefore represent a longer-term treatment option. “Why give patients a drug that leaves them vulnerable to loss of benefit?” he asks.

There appear to be high levels of compliance with patch therapy, Dr. Allen says, and good tolerability. A small percentage of patients will develop application-site reactions to the patch, he says. Roughly five to 10 percent of patients experience common side effects, which may develop over the course of therapy, Dr. Allen notes. Most patients experience symptom relief within the first two to three days after initiating therapy.

Noting that he is “excited about having a drug that allows us to have better management of RLS,” Dr. Allen suggests that rotigotine should be considered a first-line therapy option for most patients with RLS. Also presented at the AAN Annual Meeting, a post-hoc analysis of data from five, randomized, double-blind, placebo-controlled trials showed beneficial effects of rotigotine transdermal system on neuropsychiatric features and fatigue in patients with PD. Improvements were observed with rotigotine transdermal system versus placebo in items assessing apathy, anhedonia, anxiety, anxiety/depression, depression and fatigue. Individual items were identified from the scales used in these studies: the Non-Motor Symptoms Scale (NMSS), the Beck Depression Inventory (BDI-II), the 39-item Parkinson’s Disease Questionnaire (PDQ-39), the 8-item Parkinson’s disease questionnaire (PDQ-8) and the 5-item EuroQol Group questionnaire (EQ-5D).

Compared to placebo, rotigotine transdermal system was associated with improvements in:

- Depression in all three items assessing feelings of depression (p<0.02)
- Anxiety/depression in the one item assessing anxiety/depression (p<0.03)
- Anxiety in one of three items assessing anxiety (p=0.002)
- Apathy in all three items assessing apathy (p<0.04)
- Anhedonia in one of two items assessing anhedonia (p=0.026)
- Fatigue in two of three items assessing fatigue (p<0.003)

In previous studies, the rotigotine transdermal patch was shown to improve motor symptoms of PD, and in clinical practice, there was a high degree of patient satisfaction with the patch, observes Robert Hauser MD, Director, Parkinson’s Disease and Movement Disorders Center, University of South Florida in Tampa. “Parkinson’s is not just a movement...
disorder, there are a host of non-motor dysfunctions associated with the disease,” Dr. Hauser notes. In trials and clinical practice, patients seemed especially pleased with improvement in these non-motor symptoms.

The post-hoc analysis was undertaken in efforts to explore these effects. The positive findings will hopefully be further explored in a prospective trial, Dr. Hauser says.

Given that the analysis is retrospective, findings are not sufficient to drive general treatment decisions, but they may influence treatment of specific individuals, Dr. Hauser says. “Clinicians should be aware of these findings and consider them a signal…the data are sufficiently robust that, when faced with a particular patient with significant non-motor symptoms, and for whom a dopamine agonist is indicated, rotigotine may warrant additional consideration,” he notes. This is especially the case, he stresses, for those symptoms for which there is no targeted therapy: apathy, anhedonia, and to some extent fatigue.

Higher-dose Rivastigmine Patch Shows Benefits in Preservation of Function

Results of the OPTIMA trial, conducted at 140 centers in seven countries, suggest that an investigational higher-dose Exelon Patch (Rivastigmine Transdermal System, Novartis) may provide benefits in terms of preservation of function among patients with Alzheimer’s disease. The double-blind, randomized, active-comparator study, presented at the AAN Annual Meeting, was designed to compare the efficacy of the Exelon Patch 9.5 mg/24 h vs. Exelon Patch 13.3 mg/24 h in mild to moderate Alzheimer’s disease patients. The trial included an initial open-label phase of 24 to 48 weeks. Patients who demonstrated functional and cognitive decline during this time were randomly assigned to receive treatment with the Exelon Patch 9.5 mg/24 h or 13.3 mg/24 h during a 48-week double-blind treatment phase. Primary study endpoints were the change from baseline to week 48 of the double-blinded phase in function and cognition as assessed by the ADCS-Instrumental ADL (ADCS-IADL) scale and the ADAS-Cog scale, respectively.

Results showed that patients receiving the 13.3 mg/24 h patch experienced a statistically significant (p<0.05) lesser decline in function from week 16 to week 48 as compared with those using the 9.5 mg/24 h dose. Although there was a statistically significant difference in rate of decline in cognition favoring the 13.3 mg/24 h patch at week 24 (p=0.027), statistical significance was not maintained at week 48. Nonetheless, the 13.3 mg/24 h patch was numerically better on decline in cognition as compared with the 9.5 mg/24 h patch, at week 48.

Investigator Jeffrey Cummings, MD says that results of the trial were consistent with expectations, based on the initial development program for the 9.5 mg/24 h patch. The cholinergic agent is associated with predictable gastrointestinal adverse events, including nausea, diarrhea, and vomiting. Evidence from the IDEAL trial, Dr. Cummings explains, showed that the 9.5 mg/24 h patch has a more favorable side effect profile than did oral therapy with 6 mg rivastigmine BID. The investigational 17.4 mg/24 h patch had similar tolerability to the capsule. That, according to Dr. Cummings, led researchers to question, “What is the ideal balance?”

In the OPTIMA trial, Dr. Cummings points, the incidence of adverse events was not significantly different between the two treatment groups. In fact, there were fewer discontinuations due to adverse events in the higher dosage group. Still, he suspects that if the higher-dose patch comes to market, its clinical role will be as a step-up for patients who begin to decline while using the 9.5 mg/24 h patch rather than as a first-line agent for most patients.

Further studies may elucidate the difference in response to the higher-dose patch in terms of function versus cognition, Dr. Cummings says. He notes that the discrepancy may be linked to the sensitivity of the ADAS-Cog scale used in the trial.

Novartis has submitted a supplemental New Drug Application (SNDA) to expand the label for Exelon to include the 13.3 mg/24 h patch.

Study Seeks “Real World” Look at Neurotoxin Use

Intended to give a “real world” look at clinical use of onabotulinumtoxinA (Xeomin, Merz), the Phase 4, prospective, observational XCiDaBLE trial is currently underway. Initial data presented at the AAN Annual Meeting in April are based on 130 cervical dystonia (CD) and 184 blepharospasm patients enrolled in the trial as of September 1, 2011.

Eligible subjects are adults with CD or blepharospasm who a physician determines can be treated with onabotulinumtoxinA. The physician must choose to treat the patient with Xeomin prior to and independent of enrollment in the study. Although the official indication for Xeomin in blepharospasm is for patients who previously have been treated with botulinum toxin, treatment naïve patients are permitted in the trial.

Lead investigator Hubert Fernandez, MD, of the Center for Neurological Restoration at Cleveland Clinic in Ohio, notes that the study protocol did not restrict or direct patient selection other than via the criteria described above.
Additionally, there are no dosage or injection guidelines. "It’s gives us a good peek to see what clinicians do post-FDA approval of a neurotoxin," Dr. Fernandez suggests.

Initial analysis of the subjects enrolled has confirmed what would be expected of the treatment population, according to Dr. Fernandez. A majority of patients are women in their 40s to 60s. Additionally, most patients are mildly to moderately affected by their disease, with smaller numbers of the population reporting minimal or extreme effect.

One point of interest, according to Dr. Fernandez, is that about 70 percent of the blepharospasm patients and 64 percent of those with CD are no longer working because of the effects of their disease. "This suggests that we may need to re-assess our thinking on treatment and when patients receive botulinum toxin therapy," he says. "It’s possible that we are offering therapy later than these patients would have liked."

That the vast majority of blepharospasm subjects had already undergone therapy in the past with a botulinum toxin agent suggests that, even with the protocol lifting the restriction, physicians still follow FDA indications, Dr. Fernandez points out.

As more subjects are enrolled and additional analyses and sub-analyses are conducted over time, Dr. Fernandez anticipates more useful data to emerge. “The richness of this prospective observational study will come when we follow these patients over time,” he says.

Favorable New Data for Gilenya

Results from the phase III FREEDOMS extension study presented at the AAN Annual Meeting showed significant improvements in clinical and MRI measures in patients who switched from placebo (administered during the 24-month core study) to Gilenya (administered during the extension). Patients who switched from placebo to Gilenya saw a 55 percent decrease in their annualized relapse rate (ARR) during the extension phase compared to the core phase (ARR [core] = 0.29 vs. ARR [extension] 0.13; p<0.001). Significantly more patients on continuous fingolimod treatment compared to those first randomized to placebo remained relapse-free (59 percent vs. 37 percent) and free from three-month confirmed disability progression (74 percent vs. 66 percent). MRI measures showed a significantly reduced rate of brain atrophy in the patients treated continuously as compared to switch patients. The safety profile was consistent with that of the pivotal phase III trials.

The most common adverse events were nasopharyngitis, low lymphocyte counts (to be expected from the mode of action), upper respiratory tract infections and influenza.

New data for up to seven years of treatment from the phase II extension study demonstrated that patients treated with Gilenya (n=122) had sustained low MRI and clinical disease activity. The overall annual relapse rate can be expressed as one relapse every six years.

fMRI Data Elucidate Pregabalin Activity in Fibromyalgia

Findings from the first study to use functional magnetic resonance imaging (fMRI) to measure the effects of pregabalin (Lyrica, Pfizer) on brain activity in patients with fibromyalgia show that the drug decreased connectivity between various parts of the brain involved in pain processing. Findings, presented at the AAN Annual Meeting and reported by Pfizer suggested that pregabalin reduced visual activation or sensory stimulation that activates pain and affects related brain regions in patients with fibromyalgia. Pregabalin was also found to affect grey matter density in parts of the brain known to process pain. The most common adverse event in treated patients in the study compared to controls was dizziness.

Data Show Reduction in MS Disability, Relapses with Alemtuzumab

Data from the Phase III CARE-MS II trial presented in New Orleans and reported by Genzyme/Sanofi show that accumulation of disability was significantly slowed in MS patients who were treated with alemtuzumab versus high dose subcutaneous interferon beta-1a, as measured by the Expanded Disability Status Scale (EDSS). Furthermore, some patients treated with alemtuzumab showed significant improvement in disability scores from baseline and compared to patients treated with interferon, suggesting a reversal of disability in these patients. Analysis showed that patients with pre-existing disability treated with alemtuzumab were more than twice as likely to experience a sustained reduction in disability than patients given interferon.

Among the study findings:
- The mean EDSS score for patients treated with alemtuzumab decreased over a two-year period, while the mean score for patients given interferon increased (-0.17 vs. 0.24; p < 0.0001).
- At two years, 29 percent of patients treated with alemtuzumab had experienced a six-month sustained reduction in disability, compared to only 13 percent with interferon (p=0.0002).
- 65 percent of patients treated with alemtuzumab were relapse-free at two years, meaning they did not experience any relapses in the trial.