Xeomin®, a new botulinum toxin
by Daniel Truong, M.D.

Xeomin® (incobotulinumtoxinA) is a new formulation of botulinum toxin type A. It has received approval from the US Food and Drug Administration in 2010. Xeomin is approved for the treatment of cervical dystonia and benign essential blepharospasm.

Xeomin is similar to other forms of botulinum toxin type A, such as Botox® in a number of ways. It is given by injection into affected muscles. It works by blocking the release of acetylcholine. Acetylcholine is a chemical that sends messages from nerve to muscle to cause muscle contraction. Xeomin only affects the muscles at the areas injected so the muscles do not stop contracting altogether.

Xeomin is different from other forms of botulinum toxin in an important way. Other forms include both the active drug (botulinum toxin) and extra proteins. Xeomin is the first form of botulinum toxin type A that contains only the active ingredient. It does not contain any of the extra proteins. It is not clear how this difference may affect treatment, but some theories are being tested.

We recently served as an investigator in a large clinical trial of Xeomin in patients with cervical dystonia. The study was conducted at 37 clinics in the United States. The study included 233 men and women, 18-75 years of age, with cervical dystonia. Some of the patients had been treated with Botox® prior to this trial and others had never been treated with botulinum toxin.

Patients in the study were randomly assigned (by chance, like the flip of a coin) to receive one injection with 120 U Xeomin, 240 U Xeomin, or placebo. The placebo looked like the Xeomin and was injected in the same way but contained no active medication.

Before receiving the injection, at 4 weeks, 8 weeks and at the end of the study (about 20 weeks), patients completed the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS), which measures motor symptoms, disability and pain. They also completed an evaluation of overall response. Researchers rated patient improvement at each visit as well as side effects from the treatment.

The results of the study showed that both doses of Xeomin produced significantly greater improvement than placebo on the TWSTRS total score and on the motor, disability and pain subscales. Patient ratings of overall improvement were also significantly higher after

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Dear Friends of PMDF,

In our previous (summer) newsletter, I announced the beginning of my exercise program and promised a progress report in this issue. I’d like to report that I have been exercising regularly daily and have noticed a significant improvement in my symptoms and overall wellbeing. Unfortunately, that isn’t the way it went. Habits of a lifetime die hard, and I didn’t continue my program past the first day. I did attend a support group, however, and one of the things discussed was local exercise classes. I began attending a weekly dance class and a twice-weekly exercise group. These groups give me about four hours of stretching, balance, weight training, and mildly aerobic exercise each week. In addition, they get me out of the house and interacting with other Parkinson’s patients. They’re fun and good for me, a winning combination. Maybe I’ll even start doing some of the exercises at home. If you are a Parkinson’s patient or caregiver, I encourage you to seek out a nearby support group and attend meetings. You’ll meet friendly and interesting people and find out about other helpful resources.

A number of people told me that they really enjoyed the PMDF fundraiser at Los Alamitos. It was a fun evening, with good food, exciting racing, and great auction items. There are pictures later in the newsletter. Many thanks to the fundraiser committee (Ken Garrison, Karen Zent, Kellie Binder, and Paul Williams), Carol Bixby, volunteers, sponsors and donors, and all who attended for making this event successful.

Much of the money PMDF spends on research comes from the fundraiser, but individual donations are important as well. As the end of the year approaches, please consider making a donation to PMDF to improve our ability to sponsor important research on Parkinson’s disease and other movement disorders.

Have a happy holiday season!

Sincerely,

Mark Wadsworth
PMDF President
active doses of Xeomin than after placebo. Most patients reported that they had experienced “marked improvement” in symptoms over the course of the study.

The investigator ratings also showed that patients treated with Xeomin responded significantly better than those treated with placebo. Investigators rated the efficacy of Xeomin as very good or good in up to 36% of patients. They rated the treatment response to placebo as poor in 70% of patients. Xeomin was well tolerated. The most frequent side effects related to treatment were difficulty swallowing (dysphagia), neck pain and muscle weakness. Most of the side effects were mild or moderate in severity. There were no differences between groups in ratings of tolerability. Tolerability was rated as good or very good in most subjects.

Taken together, the results of the study show that both doses of Xeomin were significantly better than placebo in reducing the symptoms of CD at 4, 8, and as many as 20 weeks after a single injection.

Future studies will evaluate the safety and efficacy of Xeomin after repeated doses, and after doses that are individualized to specific patient needs.

Ask your neurologist or movement disorder specialist if Xeomin is right for you.

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Fatigue in Parkinson’s disease

by Daniel Truong, M.D.

Fatigue is a feeling of overwhelming exhaustion. It is more than just being tired; it feels like being drained of energy. Fatigue is a common symptom of many medical illnesses and it can cause disability if not managed.

Fatigue is a common symptom in patients with Parkinson’s disease (PD). It may affect as many as 56% of patients. Unfortunately, fatigue is often not recognized in patients with PD, especially in the early stage of the disease. It is important for doctors to know more about how fatigue affects patients with early PD so that they can manage it if it becomes too severe.

Dr. Giovanni Schiffitto and colleagues from the University of Rochester recently published an article in the journal Neurology that reports findings of a study on fatigue in patients with early PD. They looked at data from a larger study, the ELLDOPA (Early vs. Later Levodopa) trial. The ELLDOPA trial included both early and late stage patients with PD. Some were treated with carbidopa-levodopa for 40 weeks and others were not yet receiving medication.

In The Schiffitto study, the goal was to test the relationship between fatigue, disease severity and quality of
life. They paid special attention to patients in the study that had never been treated for their symptoms. These patients were in the early stages of PD.

Dr. Schiffitto started by looking at data from 361 patients who had been diagnosed with PD within the previous 2 years and were not likely to need medication within 9 months. Each of these patients had completed a Fatigue Severity Scale. The scale consists of 9 statements about symptoms of fatigue. Patients rated each statement on a scale from 1 (strongly disagree) to 7 (strongly agree).

Patients with scores greater than 4 were considered fatigued and those with scores less than 4 were considered nonfatigued. Dr. Schiffitto only studied the 128 patients who were considered fatigued. He looked at the relationship between fatigue and PD motor symptoms, quality of life, and activities of daily living. He also examined ratings on a depression scale. Some of the patients had also undergone brain imaging to look at dopamine receptors. The information from brain imaging was also assessed in patients with fatigue.

The results of the study showed some interesting findings. First, PD patients with fatigue were more impaired than who were not. Fatigued patients had worse score on scales of ability to do activities of daily living, motor skills, and mental ability than nonfatigued patients. There were no differences between fatigued and nonfatigued patients based on brain imaging studies.

The researchers also looked at change in fatigue over time. Specifically, they were interested in whether fatigue increased from the beginning of the study through the end of the 42 weeks. For this analysis, they compared patients who were not treated with carbidopa-levodopa to patients who were. The results showed greater increases in fatigue in patients who were not treated with medication -19%-than those who were 7 to 8%. That suggests that treatment with carbidopa-levodopa helps to reduce fatigue in patients with PD.

Overall, the results of the study show that PD patients who also have fatigue early in the disease show more severe disease and more impairment than those who do not. They also show that treatment with carbidopa-levodopa for motor symptoms can also help to reduce fatigue.

If you or a family member have PD and are experiencing fatigue, speak to your neurologist or movement disorder specialist. You doctor may be able to recommend some strategies or medications to help with your symptoms.

We would like to thank the following corporations and people for their contribution to PMDF in 2011. These contributions were given to PMDF directly and not through a fundraising campaign.

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Charles Walthall & Family
Over the years, research has linked many different behaviors and environmental influences to an increased or decreased risk of Parkinson’s disease. For example, certain pesticides and herbicides have been associated with an increased risk of disease, whereas smoking and heavy coffee drinking have been linked to a decreased risk. The problem has been that not all studies confirm these relationships, making for a “now you see it, now you don’t” phenomenon.

In attempt to understand why these relationships seem inconsistent, researchers have begun looking at differences in our genes as a possible explanation. The hypothesis is that some people may be more or less prone to disease because slight differences in our genes interact with chemicals such as nicotine or caffeine.

A recently published study has now found support for this hypothesis. The study was a collaboration among scientists in different parts of the United States and Great Britain who sought to understand the link between a person’s genes, coffee drinking, and risk of Parkinson’s disease. These scientists found that heavy coffee drinking decreases a person’s risk of developing Parkinson’s disease only if he or she has a certain type, or form, of a gene. In this study, people fell into the category of heavy coffee drinkers if they drank about 3 cups per day for 25 years or 4 cups a day for 18 years. The researchers also did some calculations that suggested it was the caffeine in coffee instead of some other chemical that was responsible for coffee’s interaction with the gene.

The gene in question provides a recipe that the body uses to make a protein known as GRIN2A. This protein helps nerve cells communicate with one another by allowing them to respond to a small chemical called glutamate. For now, no one knows exactly how one form of the GRIN2A gene interacts with caffeine to reduce the risk of Parkinson’s disease, but scientists are busy trying to find out.

Another important question is how these results help people who already have Parkinson’s disease. Will caffeine help reduce the symptoms? Many studies have already asked this question and the answer is that caffeine and caffeine-like drugs have, at most, only a minor benefit for most people with Parkinson’s disease. However, the results of the gene study raise the possibility that people with a certain form of the GRIN2A gene may benefit, whereas people with another form of the gene may not. At this point the hypothesis is speculative. But future studies may divide people up into groups based on their form of the GRIN2A gene. It may be that the group with one form of the GRIN2A gene will see improved symptoms when treated with caffeine-like drugs, whereas the group with another form of the gene may not.

Overall, the GRIN2A study is an important first step in teasing apart the interactions among a person’s genes, their habits (in this case, caffeinated coffee consumption), and Parkinson’s disease. This study will almost certainly be followed by others of its kind looking at different genes, behaviors, and environmental factors. Eventually, this work could lead to genetic tests that help us determine which treatments will work best for each individual patient. This gene-based strategy has already led to substantial advances in cancer therapy, and may lead to more personalized, targeted treatments for Parkinson’s disease as well.
We would like to thank the following for their contributions to the PMDF Fundraiser in 2011.

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OUR MISSION

To support basic and clinical research into the causes, treatments and cures for Parkinson’s disease and other movement disorders such as dystonia, myoclonus, spasticity, and tremor.

The Parkinson’s and Movement Disorder Foundation is committed to working with other organizations that have similar philosophies in an effort to bring together expertise from both basic and clinical science perspectives.

We are dedicated to enhancing the quality of life for those who suffer from movement disorders and their families, through research, education, and community outreach.