

ADAGIO Phase III Trial of Rasagiline: An update



In our last newsletter, we announced preliminary word of positive results from the ADAGIO phase III study. This study was designed to test the hypothesis that rasagiline (marketed as Azilect® in the United States and European Union by Teva Pharmaceuticals) would slow the progression of Parkinson's disease. The 18-month study, the first of its kind, was one of the largest conducted in Parkinson's disease, involving 1,176 patients with early Parkinson's disease in 14 countries and 129 medical centers, including Pacific Neuroscience Medical Group.

On September 19, 2008, TEVA pharmaceuticals convened a meeting of the investigators in this landmark

trial in Miami, Florida, in order to present the results.

About the study

Patients in this trial were randomized to early-start treatment (72 weeks rasagiline 1 or 2 mg once daily) or delayed-start treatment (36 weeks placebo followed by 36 weeks rasagiline 1 or 2 mg once daily). The primary analyses of the trial were based on change in total UPDRS (Unified Parkinson's Disease Rating Scale) and included slope superiority of rasagiline over placebo in the placebo-controlled phase, change from baseline to week 72, and non-inferiority of early-start vs. delayed-start slopes during weeks 48-72 of the active phase. The UPDRS is the most commonly used rating scale to assess disease status.

Results

The group of patients ran-

(Continued on page 2)

From the Medical Director



Welcome to the inaugural issue of our new newsletter! For those of you wondering what happened to "The Brainiac," we planned to make a few improvements, but by the time we were through, we had changed so much that it seemed like a good idea to start afresh with a completely new look as well as a new name!

Why "The Synapse?" The synapse is the part of the nervous system where information is transferred from one brain cell to the next. In the same way brain cells communicate with each other, we want to communicate the latest and most exciting news about the brain, neuroscience research, and our center to you, our friends and colleagues.

We have also added new features and expanded the number of articles. Finally, in order to make our newsletter more accessible, we have decided to produce it in a PDF format, easily downloadable. Please feel free to print as many copies as you want and share them with your family and friends!

Yours truly,


James P. Sutton, MD

Google Co-founder Announces He Carries the Parkinson's Gene

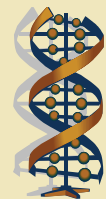


Last month, [Sergie Brin](#), co-founder of Google, announced to world in his inaugural blog that he carries the LRRK mutation that has been shown to be causative for Parkinson's disease (PD) in Ashkenaze Jews and other groups. Although he has no symptoms of Parkinson's dis-

ease at this time, his mother and aunt both have PD and were found to carry this mutation. His risk of developing Parkinson's disease at some point in his life is not known, but may be anywhere from 20 to 80%. His decision to make his own test results public is remarkable, both for the courage he has displayed in sharing something so personal, and for the hope that it has now given to hundreds of thousands of people living with or at risk of developing Parkinson's dis-

ease. Not only has he brought attention to the importance of genetic research for PD, he has brought attention to the remarkable breakthroughs in the genetics of all neurological disease that have come to light in the past decade. For further information about the LRRK mutation and research on the genetics of Parkinson's disease, take a look at the [LRRK page on "Online Mendelian Inheritance in Man \(OMIM\)](#). This site, aimed at scientists and physicians, has a wealth of information about this important area of research.

Inside this issue:



AMT Obtains License to Amgen's GDNF Gene to Develop Treatment for Parkinson's Disease

page 3

Underlying Cause of Pneumonia Common in Parkinson's Disease Patients

page 3

Current Clinical Trials at Pacific Neuroscience Medical Group

page 4

Alzheimer's 2008: a Caregiver and Patient Conference

page 4

APDA Ride for a Cure

page 4

ADAGIO

(Continued from page 1)



"This is an extremely exciting result, and one that will most likely change the way we treat early PD"

- James P. Sutton, MD

domized to early-start treatment with rasagiline 1 mg a day met all three primary analyses. The slopes of the group receiving rasagiline compared to the group receiving placebo were 0.14 UPDRS points per week compared to 0.09 UPDRS points per week between months 3 and months 9. **This is equivalent to a 36% reduction in the rate of progression in the group receiving rasagiline 1 mg a day.** In addition, the group that began to receive rasagiline 1 mg at month 9 never caught up to the group that received rasagiline at study start, suggesting that the effect was neuroprotective rather than simply symptomatic. Finally, the rate of progression of illness from month 12 to month 18 was identical in both groups; in other words, there was no "catch-up" effect in those patients who had previously shown a slower rate of progression.

Results for the 2 mg arm of the study were somewhat harder to interpret, as not all of the endpoints were met in this group. One possibility is that the symptomatic effect for patients in the 2 mg group was larger than expected, and this may have masked the neuroprotective effect. It is likely that experts will debate the finer details of this part of the study for a long time to come, however, there is no denying the significance of the results seen in the 1 mg group.

What does this mean?

"It may be premature to conclude that rasagiline 1 mg a day has a true neuroprotective effect, however, it is diffi-

cult to explain the results of this study in any other way" according to James P. Sutton, Principal Investigator for this study at Pacific Neuroscience Medical Group. "There remain many unanswered questions, such as whether or not this neuroprotective effect diminishes, persists, or increases later in the course of the illness. In addition, this study has to be interpreted cautiously for patient with later stages of illness, as the patients in this study were on average only diagnosed with PD 4 months before they entered the study. Nevertheless, this is an extremely exciting result, and one that will most likely change the way we treat early PD"

What are the side effects?

In this study of patients who were not on dopaminergic therapy for Parkinson's disease at entry, side effects were the same in the patients receiving study drug compared to patients receiving placebo. However, in other studies of this medication, especially in studies of patient with more advanced illness on multiple PD medications, side effects were more common than placebo. Among other side effects, two in particular stood out in an analysis performed by Chris Goetz in collaboration with the PRESTO study group. These included increased dyskinesias in younger patients having this problem, and hallucinations in older patients. Although the results were deemed not statistically significant, they are open to interpretation, suggesting caution when using this medication in patients with more advanced illness.

Are there any other precautions to be aware of?

Despite the demonstrated safety in the ADAGIO and other studies, the labeling for rasagiline still includes many dietary and medication restrictions. In addition, you need to consider the cost of the medication. The FDA has not approved rasagiline for anything other than symptomatic therapy, and your insurance company may not cover the cost of using it as a neuroprotective agent.

What might the difference in rate of progression mean for my quality of life?

This question is very difficult to answer, as the study only addresses a six month period; the difference during that time in UPDRS scores was understandably not great. However, if the effect persists, this could mean a significant difference in quality of life years down the road for patients who begin therapy with rasagiline early. The key word, however, is "if."

Should I start on rasagiline?

Perhaps. We recommend that each patient with PD is learn as much about the potential risks and benefits of adding this medication before making such a decision. In addition, this is a decision that should only be made in consultation with a neurologist knowledgeable about Parkinson's disease and the detailed results of the ADAGIO and related studies.

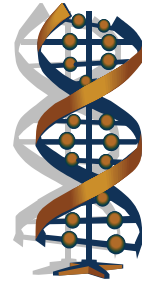
Amsterdam Molecular Therapeutics (AMT) Obtains License to Amgen's GDNF Gene

[Amsterdam Molecular Therapeutics](#), a leader in the field of human gene therapy, recently announced that it has obtained a license from Amgen to use their Glial Derived Neurotrophic Factor (GDNF) gene for the development of a gene therapy treatment for Parkinson's disease.

GDNF is a protein necessary for the development and

survival of nerve cells. The positive effect of GDNF on nerve cells has been shown in several animal studies, making it an attractive candidate for the treatment of Parkinson's disease. Unfortunately, early attempts to deliver the GDNF protein to the necessary areas of the brain have been limited, and early clinical trials have not been

successful. AMT will combine the GDNF gene with their own proprietary adeno-associated virus (AAV) gene therapy platform, potentially providing a solution for delivering GDNF to the brain. If successful this would allow the development of a novel effective, long-term neuro-protective treatment for Parkinson's disease.



Underlying Cause of Pneumonia Common in Parkinson's Disease Patients



Impaired coordination between breathing and swallowing may be the underlying cause of aspiration pneumonia in Parkinson's patients, report researchers from the [otolaryngology department of the University of Pittsburgh School of Medicine](#) in a recent issue of the journal "Dysphagia."

At least half of all Parkinson's patients report having difficulty swallowing, and a higher percentage show swallowing abnormalities on X-ray tests. This can lead to the inhalation of food and drink at mealtime, resulting in what physicians call "aspiration." Aspiration can in turn cause an infection of the lungs known as "aspiration pneumonia." Aspiration pneumonia is a leading cause of hospitalization for individuals with Parkinson's

disease. The high prevalence of swallowing problems and risk of aspiration in patients with Parkinson's disease may be largely due to flawed breathing and swallowing patterns, according to the researchers.

While the underlying cause of swallowing problems in Parkinson's has not been well understood, prior research has found that healthy adults swallow most often during exhalation and that exhalation regularly follows the swallow, even when a swallow occurs during inhalation. Dr. Gross's study looked at Parkinson's patients as they swallowed standardized portions of pudding and cookies. While participants spontaneously ate, researchers measured their nasal airflow and respiratory movement to determine where swallowing took place in the respiratory cycle. They found that Parkinson's patients inhale during and after swallowing significantly more often than healthy adults. Also, the Parkinson's patients swallowed at

low lung volumes more often than the healthy adults.

The findings indicate that swallowing problems may be respiratory-based as well as neuromuscular-based. This may help to explain why Parkinson's medications do not consistently help to improve swallowing function.

"Most Parkinson's patients don't know they have swallowing problems - even though aspiration pneumonia often is a severe complication of the disease - and Parkinson's drugs most often do not improve these patients' swallowing function," said Roxann Diez Gross, Ph.D., principal investigator. "Now that we know the respiratory system may play an important role in swallowing problems in patients with Parkinson's disease, we can develop therapies to help these patients re-coordinate breathing and swallowing patterns to improve swallowing function and possibly avoid aspiration pneumonia."

"Now ... we can develop therapies to help these patients re-coordinate breathing and swallowing patterns to improve swallowing function and possibly avoid aspiration pneumonia."

the synapse



Current Clinical Trials at Pacific Neuroscience Medical Group

We are currently seeking volunteers with Parkinson's disease, orthostatic hypotension, Alzheimer's disease, partial epilepsy, or post-herpetic neuralgia for our

clinical trials program. We will be starting a clinical trial for patients with fibromyalgia later this year, and we are currently reviewing additional proposals from several phar-

maceutical companies. For further information about our clinical research program, please call us at 805-278-4148 or visit us online at www.thisisyourbrain.com.

Alzheimer's 2008: a Caregiver and Patient Conference

In recognition of Alzheimer's Awareness Month, Pacific Neuroscience Medical Group and the [Central Coast Chapter of the Alzheimer's Association](#) will be co-sponsoring a patient and caregiver symposium for those affected by this illness. Pacific Neuroscience Medical Group has held similar events for Parkinson's disease and Alzheimer's disease since 2004. This marks the third annual conference for Alzheimer's Awareness, and the first year that the event will be co-hosted by the Alzheimer's association. The event will be held at the Marriott Esplanade in Oxnard; for details, please see the full program on page 5 or visit us online at www.thisisyourbrain.com.

About Alzheimer's disease

Alzheimer's disease (AD), also called simply Alzheimer's, is

the most common form of dementia. Generally it is diagnosed in people over 65 years of age, although the less-prevalent early-onset Alzheimer's can occur much earlier. An estimated 26.6 million people worldwide were afflicted with Alzheimer's in 2006; this number may quadruple by 2050. Although each sufferer experiences Alzheimer's in a unique way, there are many common symptoms. In the early stages, the most commonly recognized symptom is memory loss, such as difficulty in remembering recently learned facts. When a doctor or physician has been notified, and AD is suspected, the diagnosis is usually confirmed with behavioral assessments and cognitive tests, usually followed by a brain scan if available. (source: wikipedia.com).

About the Alzheimer's Association

The Alzheimer's Association provides supportive programs and services to help people with Alzheimer's and their caregivers deal with the disease and its impact on their lives. Each chapter in their nationwide network offers five core services: information and referral, care consultation, support groups, safety services, and education. In addition, some chapters offer special programs such as assistance to individuals with Alzheimer's who live alone, people living with early-onset Alzheimer's, rural and/or multicultural outreach, care coordination services, and training programs for families and professionals. For further information, visit the Alzheimer's association online at www.alz.org.

"An estimated 26.6 million people worldwide were afflicted with Alzheimer's in 2006"

American Parkinson's Disease Association and the Ride for a Cure

On October 4, 2008, the Gibson Ranch in Sunland, California together with ETI Corral 210 hosted the grand finale of the second annual **Ride for a Cure**, to support outreach and research for Parkinson's disease and cancer. This event began as a small independent non-profit fundraiser in 2007. The brainchild of the event, Jo Martinetti, is a long-

time Parkinson's advocate, Parkinson's patient and equestrian.

Thanks to the remarkable energy and compassion of a small group of ordinary people and equestrians, this grew from a one day fundraising event to a festival spread over three weekends. Money was raised for both the American Parkinson's

Disease Association (APDA) San Fernando Valley Regional Chapter, as well as the new Roy and Patricia Disney Cancer Center at Providence Saint Joseph Medical Center in Burbank. Dr. Sutton represented Pacific Neuroscience Medical Group at the event. For more information about the

(Continued on page 5)



Alzheimer's 2008

[Courtyard by Marriott Oxnard/Ventura](#)

600 Esplanade Drive
Oxnard, CA 93036

Reservations: 805-278-4148 or information.request.2008@pacificneuroscience.com



Program

- 8:30 AM Registration**
- 9:00 AM Welcoming remarks and Introduction**
James P. Sutton, MD, Pacific Neuroscience Medical Group
- 9:15 AM The Neurology of Alzheimer's Disease**
Robert Harbaugh, MD, Neurology Associates of Santa Barbara
- 9:45 AM The Psychiatry of Alzheimer's Disease**
Jerry Bruns, MD, La Mer Medical Group
- 10:15 AM The Neuropsychology of Alzheimer's Disease**
Steven Rogers, PhD, Pacific Neuroscience Medical Group
- 10:45 AM Break**
- 11:00 AM Keynote Address: From the Laboratory to the Clinic: the Search For a Cure**
Ken Kosik, MD, UCSB Neuroscience Research Institute
- 11:45 AM Clinical Research for Alzheimer's Disease: the EPIX and LILLY studies**
Jason Fajardo, PA-C, Pacific Neuroscience Medical Group
- 12:00 PM The Alzheimer's Association: Who We Are and What We Do**
Norma Featherston, RN, MS, Ventura County Alzheimer's Association
- 12:15 PM Panel discussion**
- 1:00 PM Conclusion**

Ride for a Cure

(Continued from page 4)

San Fernando Valley Regional Chapter of the APDA, or to make a donation to support their mission, please visit their website at www.valleyparkinsons.org.



Left:
opening
parade
from the
Ride for a
Cure 2008

Other upcoming events of interest*

October 18, 2008: "Memory Walk 08," a fundraiser. Thousand Oaks. (Alzheimer's Association)

October 18, 2008: "Pancakes for Parkinson's," a fundraiser. Westlake Village. (APDA)

October 25, 2008: "PD 101," a class on the basics of PD. Northridge Hospital. (APDA)

October 25, 2008: "Put the Fire Out for Parkinson's," a 2-mile fund-raising walk. Camarillo. (TeamFOX)

*(*these events are educational and/or fund-raising events of interest to our patients and friends. This information is provided as a public service, and should not be considered an endorsement of any specific event or events. For further information such as times, locations, and contact information, or to have your event listed in our next newsletter, please call us at 805-278-4148. In the future, we hope to include more detailed information here for the benefit of our community.)*

published bimonthly by Pacific Neuroscience Medical Group, Inc. ▼ All rights reserved. ▼ contents © 2008 Pacific Neuroscience Medical Group, Inc. ▼ address correspondence to: Pacific Neuroscience Medical Group ▼ 1701 Solar Drive, Suite 140, Oxnard, CA 93030. ▼ phone: 805-278-4148 ▼ fax: 805-278-4634 ▼ e-mail: information.request.2008@pacificneuroscience.com. ▼ visit us online at : www.pacificneuroscience.com or www.thisisyourbrain.com.