Journal article on the Phase II trial of Dimebon has been published

Dr. Karl Kieburtz and colleagues have published a journal article on the Phase II trial of Dimebon which was completed in the summer of 2008. In July 2008, we reported on the promising results of the Phase II clinical trial of Dimebon (Dimebon found safe and well-tolerated with indications of effectiveness). We can now provide more details.

The drug is now being referred to as latrepirdine. The Phase II trial involved 91 participants with mild to moderate Huntington's Disease. Participants took 20 mg of latrepirdine or a placebo three times a day in a randomized double blind study lasting 90 days. The trial was sponsored by Medivation and administered by the Huntington Study Group.

The purpose of a Phase II study is to ascertain safety and tolerability but researchers also look for any indications of effectiveness. Latrepirdine was found to be safe and well tolerated in this short trial with 87 percent of the treatment group completing the study compared to 82 percent of the placebo group. Any adverse medical event is reported, whether or not it is thought to have a connection to the study. 70 percent of those taking latrepirdine and 80 percent of those taking the placebo reported adverse events.

The other good news is that they did find an indication of effectiveness as well as some promising trends. The treatment group experienced cognitive improvement as measured by the Mini-Mental States Examination, a broad measure of cognition. The difference was statistically significant ($p < .03$).

There were no meaningful differences on the Alzheimer's Assessment Cognitive Subscale nor on the cognitive subscales of the United Huntington Disease Rating Scale. This raises the issue of how best cognitive changes can be measured in Huntington's trials. Alzheimer's is a cortical dementia whereas Huntington's is primarily a subcortical dementia. The UHDRS was designed to measure changes in a slowly progressive disease over time in a clinical setting.

Two trends that were not statistically significant are intriguing and it will be interesting to see if they become significant in the larger Phase III trial. First, behavioral outcomes were better for the latrepirdine group as measured by the UHDRS.

Second, falling was the most commonly reported adverse event, not surprising in Huntington's patients. However only 9 percent of the treatment group experienced falls compared to 16 percent of the placebo group. Again, this was not statistically significant in this small trial.

A double blind trial of latrepirdine in 183 mild to moderate Alzheimer's patients produced a statistically significant improvement in cognition in the treatment group as compared to the placebo group. In addition, the drug was well tolerated for the twelve months of the Alzheimer's trial.

The authors concluded that a Phase III (final) trial of latrepirdine was warranted and one is now enrolling. For more information about the trial click here: http://www.horizontrial.com/

For a list of participating sites and contact people, click here: http://www.huntington-study-group.org/Portals/0/HORIZONSiteList.pdf

"We are encouraged about the DIMOND results, and by the community's interest in the HORIZON trial. The study team is committed to helping interested people to learn more about the study, and to possibly participate, if appropriate for them!" said Dr. Kieburtz.

References:

Rachelle S. Doody, Svetlana Gavrilova, Mary Sano, Ronald G. Thomas, Paul S. Aisen, Sergey O. Bachurin, Lynn Seely, and David Hung, on behalf of the Dimebon investigators. "**Effect of dimebon on cognition, activities of daily living, behaviour, and global function in patients with mild-to-moderate Alzheimer's disease: a randomised, double-blind, placebo-controlled study."** The Lancet Vol. 372:9634(19 July 2008):207-215.

Karl Kieburtz, Michael P. McDermott, Tiffini S. Voss, Jody Corey-Bloom, Lisa M. Deuel, E. Ray Dorsey, Stewart Factor, Michael D. Geschwind, Karen Hodgeman, Elise Kayson, Sarah Noonberg, Michael Pourfar, Karen Rabinowitz, Bernard Ravina, Juan Sanchez-Ramos, Lynn Seely, Francis Walker, Andrew Feigin, and The Dimebon in Subjects With Huntington Disease (DIMOND) Investigators of the Huntington Study Group. "**A Randomized, Placebo-Controlled Trial of Latrepirdine in Huntington Disease."** Archives of Neurology 2010;67(2):154-160.

- Marsha L. Miller, Ph.D., February 9, 2009