

Dimebon and Alzheimer's

Pharmaceutical companies are taking a new interest in Huntington's Disease. This welcome development means that it often takes a while before journal articles about the supporting research behind the drug are published. Pharmaceutical companies want to avoid alerting competitors to their early drug development efforts.

Medivation has added Huntington's Disease trials to its trials of Dimebon in Alzheimer's Disease (AD). Following good results with a Phase II HD trial, a final phase III trial is now in the planning stages while a Phase III trial in AD is already underway. While the HD community awaits publication of all of the results in the newly ended Phase II trial, a newly published article in the Lancet is giving us our first look at what all the excitement has been about with Alzheimer's clinical trials.

The Lancet article, along with a 2001 article published in the New York Annals of Science, reports on the Russian research with Dimebon. Dimebon is an antihistamine developed in Russia two decades ago. Newer antihistamines have replaced it but the drug itself appeared to have neuroprotective effects, which led to its investigation as a potential Alzheimer's treatment.

The 2001 article reported on studies with a cell model of Alzheimer's, a neurotoxin rat model, and human subjects, all of which yielded promising results. Fourteen patients were given Dimebon in an open label trial. Improvement was found in cognitive, psychiatric, and functional measures.

When the word 'improvement' is used in preclinical or clinical trials, the investigators are referring to a better result on for the treatment group as compared to a control group or results from observational studies of the disease. 'Improvement' may simply mean a slower decline than is expected in a neurodegenerative disorder. However, in the open label trial, the symptoms of the patients receiving Dimebon actually improved.

The new article in the Lancet reports on a placebo controlled double-blinded study with 183 patients with mild to moderate AD. Half of the participants received Dimebon and half the placebo. Neither the participants nor those evaluating them in the year-long study knew who was in which group. Measured were thinking and memory ability, overall function, psychiatric and behavioral symptoms, and ability to perform daily activities.

"More research is needed, but we are encouraged by the effect the drug Dimebon had on Alzheimer's patients" said Dr. Rachele Doody, professor of neurology at Baylor College of Medicine and lead author of the study. "What we saw in the clinical trial is that people on the medication continued to improve over time," Doody said. "Those on placebo continued to decline."

Remarkably, patient improvement was found across the board in the treatment group. "Usually at this point in a drug's development, we are happy to see improvement in one of the outcome measures," Doody said. "We saw improvement in all five."

This is wonderful news for those with Alzheimer's and researchers are hoping to see the results confirmed in the larger, multi-centered Phase III trial that is now underway.

The results may also be good news for the HD community if Dimebon is addressing a pathological mechanism common to both AD and HD. We are waiting for animal research to be published sometime this year to learn more but according to Medivation, they have good evidence to suggest that Dimebon stabilizes mitochondria. Mitochondria are not managed properly in HD and impaired energy metabolism appears to be a major problem so Dimebon would appear to hold promise for Huntington's Disease patients as well. The results of a Phase III trial, now in the planning stages will answer the question.

References:

Baylor College of Medicine press release

S Bachurin, E Bukatina, N Lermontova, S Tkachenko, A Afanasiev, V Grigoriev, I Giigorieve, Yu Ivanov, S Sablin, and N Zefirov. "Antihistamine agent Dimebon as a novel neuroprotector and a cognition enhancer.." **Annals of the New York Academy of Sciences** **939(2001):425-435.**

R Doody, S Gavrilova, M Sano, R Thomas, P Aisen, S Bachurin, L Seely, D Hung. "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* , Volume 372 , Issue 9634: 207-215.

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