

Non-stimulant Drug Effective in Adult ADHD

MG01CI, an extended release formulation of metadoxine, meets primary endpoint in a phase II randomized clinical trial of patients with ADHD.

Petia Gatzeva-Topalova, PhD

September 9, 2011 –MG01CI, a novel non-stimulant drug, showed improvement of symptoms in adults with attention deficit hyperactivity disorder (ADHD), according to results from a randomized placebo-controlled phase II clinical study.

Results of the study were announced by Teva Pharmaceutical Industries Inc. and Alcobra Ltd this week in a written release.

MG01CI is a slow-release metadoxine formulation. Metadoxine is approved in some countries to treat acute and chronic alcohol intoxication. Studies, however, have shown that metadoxine also affects the serotonin receptor family. Serotonin levels have been previously linked to ADHD.

A phase I study of MG01CI devised to evaluate the general safety of the drug showed no adverse effects. The larger phase II study was designed to determine the efficacy, as well as safety, of MG01CI as compared with placebo. The Phase II study consisted of three periods: 1) a 2-week screening period prior to dosing; 2) a 6-week double-blind treatment period; 3) a 2-week safety follow-up period.

A total of 120 patients were randomized in a 1:1 ratio to two treatment groups. The active group received a daily dose of 1400 mg MG01CI, while the control group received placebo. Evaluation of the groups was based on Conners' Adult ADHD Rating Scale-Investigator Rated Total ADHD Symptoms Score (CAARS-INV), the Adult ADHD Quality-of-Life (AAQoL) Scale, the Clinical Global Impression (CGI) scale, and the Test of Variables of Attention (T.O.V.A.®) test.

Results of the phase II clinical study showed significant benefit from MG01CI in the active group as compared with control ($P<0.03$). Of the participants, 56% in the active group showed an improvement of 25% in their CAARS-INV score after treatment with MG01CI. Similar improvement of 25% in the CAARS-INV score was observed in only 36% of the control group patients ($P<0.03$).

An even greater improvement of more than 40% in their CAARS-INV was documented for 44% of the patients in the treatment arm vs. 25% in the placebo-treated group ($P<0.04$). MGO1CI also exhibited improvement in additional tests, including AAQoL and T.O.V.A.® scores.

Adverse effects from MG01CI included nausea and insomnia. However the rate of patients refusing treatment because of the side effects was similar between the active and the control groups (1.7%).

In addition, no increase in blood pressure or appetite suppression was observed as a result of treatment. Blood pressure increase and appetite suppression, among others, are common side effects for standard ADHD treatment with stimulants, and many experts are reluctant to prescribe those treatments for extended periods of time.

"I am very encouraged by the results of this trial, which warrants further clinical development of MG01CI, a novel non-stimulant drug that may benefit many people with ADHD", said Iris Manor MD, director of the ADHD Unit, Geha Mental Health Center in Petach Tikva, Israel, in a press release today.

Dr. Yaron Daniely, CEO of Alcobra stated in a press announcement that "these results confirm previous clinical experience indicating MG01CI may have a quick onset of activity with few side effects, distinguishing it from other non-stimulant ADHD treatments. Based on the positive results of this phase II

trial and the high unmet need for novel ADHD treatments, we intend to commence phase III studies in adults in 2012 and later on in children.”