Antinarcoplyse Drug May Improve ADHD

Modafinil could prove an alternative to stimulants for addressing symptoms, phase III studies show.

By Mary Ellen Schneider

Atlanta — Results from new research point to a possible alternative to stimulants for the treatment of attention-deficit hyperactivity disorder (ADHD) in children and adolescents.

Two phase III studies presented at the annual meeting of the American Psychiatric Association show that a once-daily pediatric formulation of modafinil is well tolerated and improves attention deficit hyperactivity disorder (ADHD) symptoms in children and adolescents.

Modafinil is currently marketed by Cephalon under the brand name Provigil in 100-mg and 200-mg strengths. Provigil is indicated for the treatment of excessive sleepiness associated with narcolepsy, obstructive sleep apnea, hypopnea syndrome, and shift work sleep disorder.

The company, which funded the phase II trials, is seeking approval from the Food and Drug Administration to market modafinil in 85-mg, 170-mg, 255-mg, 425-mg, and 425-mg strengths. If approved, the results could be indicated for treatment of ADHD in children and adolescents aged 6-17 years.

The company is planning to launch the drug under the brand name Attenace by early 2006.

In one study, 189 patients with ADHD aged 6-17 years were randomized to a 7-week double-blind, fixed-dose treatment with either modafinil or placebo. This protocol was followed by a 2-week withdrawal period in which half of the modafinil-treated patients were placed on placebo without tapering, and half were continued on the drug, said Joseph Biederman, M.D., the lead investigator in the study and professor of psychiatry at Harvard University in Boston.

Modafinil was administered once daily, starting at 85 mg/day, and was rapidly titrated over 7.9 days to dosages of either 340 mg/day for patients who weighed less than 30 kg or 425 mg/day for patients who weighed 30 kg or more.

The results of the study were assessed using the school and home ADHD Rating Scale IV total score change from baseline to last treatment visit.

After 1 week, the 125 modafinil-treated patients had significantly greater improvements in school scores, compared with the 64 placebo patients, and those results were maintained through week 7.

On the school scale, patients on modafinil experienced a 17.2-point drop in symptoms, compared with an 8.2-point drop for patients on placebo. Modafinil also significantly improved total scores from parents, compared with placebo.

The side effects were generally mild and occurred at initiation of the treatment. There were two serious adverse events not associated with the trial, said Dr. Biederman, who is an advisory board member for Cephalon and receives research/grant support from the company.

The researchers also assessed ADHD symptoms and physical/emotional response after rapid discontinuation. During the 2-week withdrawal phase there were no reported symptom rebounds, no adverse events related to withdrawal, and no physical or emotional responses.

Modafinil appears to work like a gentler stimulant, Dr. Biederman said in an interview. Studies have shown that modafinil-treated patients were placed on placebo without tapering, and half were continued on the drug, said Joseph Biederman, M.D., the lead investigator in the study and professor of psychiatry at Harvard University in Boston.

Modafinil was shown to significantly improve attention-deficit/hyperactivity/impulsivity, and there was an improvement in overall clinical condition and in the TOVA measurements of ADHD.

The researchers focused not only on decreasing symptoms of ADHD, but on increasing positive interaction and social skills, and they saw an increase in positive behaviors, he said.

Side effects included insomnia, headache, and appetite decrease. Overall, the side effects were generally mild and occurred at initiation of the treatment. There were two serious adverse events not associated with the trial. Dr. Biederman, who is an advisory board member for Cephalon and receives research/grant support from the company, and is a member of the company’s speakers’ bureau.

Conduct, Bipolar Disorder Often Comorbid With ADHD

By Heidi Spletz

Houston — When I ask whether I think [attention-deficit hyperactivity disorder] is overdiagnosed, I say yes, Dr. Gillllian, D.O., said at the annual meeting of the American Society for Adolescent Psychiatry. “Did we miss ADHD before? No, the hyperactive kids wore themselves out,”

When Dr. Gillllian assessed children and adolescents with ADHD meet criteria for a related category disorder, oppositional defiant disorder, and bipolar disorder.

When evaluating a child or adolescent for ADHD, it is important to consider other conditions as well. When Dr. Gillllian assessed children and adolescents with ADHD, with or without comorbidities, she starts by asking parents about the child’s behavior.

Hyperactive children were often very active in uttero and active as infants; they didn’t sleep well and were distracted when eating, she said. In addition, children with ADHD often skipped the crawling stage or spent very little time crawling. Dr. Gillllian also asks whether the child or adolescent is invited to birthday parties.

It’s very a big developmental thing on the social side, and parents who recognize a “hyper,” aggressive child may not want the child in their house, she noted.

She also asks about emergency department visits and car accidents.

“I like to look at report cards, to see what teachers wrote about behavior,” she said. Another question is who babysits. “If the grandmother won’t babysit the child, then that’s a problem.”

People do not truly outgrow ADHD; motor hyperactivity in childhood evolves into internal feelings of restlessness in adolescence and adulthood.

Conduct disorder. “I call these the thugs and ‘thugs,”’ Dr. Gillllian said. “These children or teens have a disrespect for societal norms—they genuinely do not care about the rights of others. The majority of child-onset cases of conduct disorder are treated by adolescence the numbers are approximately equal. Children with conduct disorder don’t always make it to the psychiatry because they go into the legal system first.

Oppositional defiant disorder. By contrast, children with oppositional defiant disorders tend to be argumentative, but usually only within their immediate network of family and friends. Some kids negotiate that way, some derive satisfaction from engaging their parents in an argument.

Bipolar disorder. More than 50% of adolescents with bipolar disorder have at least one coexisting psychiatric disorder.

“In many areas, to get a child some time in a psychiatric hospital, you must have a diagnosis of bipolar disorder,” Dr. Gillllian noted. As a result, many clinicians lead with the bipolar diagnosis because they know the child needs to spend some time in an inpatient hospital. Features of bipolar disorder in children and adults are similar to characteristics of ADHD. The prolonged outbursts, which she described as “affective storms,” are bipolar rather than hyperactive.

Early symptoms of childhood-onset bipolar disorder include refractoriness to sensory stimulation and night terrors as an infant, and high levels of anxiety and difficulty controlling anger as a school-aged child. Reports from family members might suggest that the child has a difficult temperament.

Treatment options for children and adolescents with ADHD and other conditions include Strattera (atomoxetine), Adderall (amphetamine mixed salts), and Concerta (methylphenidate HCI) and Daypro (dextroamphetamine sulfate). Underdosing is one of the most common reasons for discontinuing medication. Dr. Gillllian said. Parents often are not used to titrating their children’s medications, since it is not used for ear infections or urinary tract infections.

Families become impatient and say that the medication is not working; they may want to switch drugs instead of increasing the dose. “Medication can do some things, but other things must be done at the same time,” she said. Nonmedication therapies for ADHD and bipolar problems include hobbies, sports that channel energy, and strategies for better academic performance, said Dr. Gillllian, a consultant and member of the speakers’ bureau for Pfizer, Ortho-McNeil, and Abbott, and a member of the speakers’ bureau for AstraZeneca.

People do not truly outgrow ADHD; motor hyperactivity in childhood evolves into internal feelings of restlessness in adolescence and adulthood.