Varenicline Bolsters Cessation in COPD Patients

BY BRUCE JANCIN

SAN DIEGO — Varenicline is a particularly effective and well-tolerated smoking cessation therapy in one of the toughest-to-treat of all groups: long-time smokers with chronic obstructive pulmonary disease.

That was the key finding in a 27-center, randomized, double-blind, placebo-controlled trial involving 499 highly nicotine-dependent subjects with mild to moderate COPD and an average 41-year history of smoking, Dr. Donald P. Tashkin said at the annual meeting of the American College of Chest Physicians.

Participants were randomized to 12 weeks of varenicline (Chantix) at 1 mg twice daily or placebo and were followed out to 52 weeks in the blinded post-treatment phase of the trial. All subjects received smoking cessation counseling throughout the study.

The primary study end point was continuous abstinence during weeks 9-12—the last month of therapy—as confirmed by exhaled carbon monoxide measurements. This was achieved by 43% of the varenicline group and 9% of controls, reported Dr. Tashkin, emeritus professor of medicine at the University of California, Los Angeles.

The major secondary end point was continuous abstinence during weeks 9-52. This was accomplished by 19% of the varenicline group, a success rate more than triple the 6% figure among controls.

Serious adverse events occurred in 2.8% of varenicline-treated patients and 4.4% of controls.

There was no difference between the two groups in the incidence of depression or other psychiatric disorders; however, patients with serious mental illnesses were not eligible to enroll in the study.

The most common adverse events associated with varenicline were nausea, reported by 27% of treated patients compared with 8% of controls, and abnormal dreams, reported by 11% on varenicline and 3% on placebo.

Study participants averaged 24 cigarettes per day at baseline. Eighty percent had previously made one or more unsuccessful attempts to quit. Their mean 6.1-point score on the 10-point Fagerström Test for Nicotine Dependence was indicative of their high level of nicotine dependence.

Dr. Tashkin noted that more than 12 million Americans carry the diagnosis of COPD, and 80%-90% of them are smokers. Treatment guidelines from the Global Initiative for Chronic Obstructive Lung Disease identify smoking cessation as the single most effective intervention both in preventing the development of COPD as well as in slowing progression of the disease.

"I would think that varenicline would be first-line therapy for patients with COPD who continue to smoke," Dr. Tashkin said in an interview. "This is a very effective—probably one of the most effective—treatment strategies to help smokers with COPD quit."

He was the lead investigator in an earlier double-blind, placebo-controlled, randomized trial that established sustained-release bupropion as a safe and effective aid in helping smokers with COPD to quit (Lancet 2001;357:1571-5).

Dr. Tashkin is a consultant to Pfizer, which sponsored the varenicline study. ■

MY TAKE

Don't Overlook the Power of Counseling

Chronic obstructive pulmonary disease causes prolonged suffering. And because patients with COPD are notoriously refractory to stopping smoking, this report should offer hope.

However, I agree with my colleague John Polito, creator of the nonprofit Web site www.whyquit.com, to which I refer all my patients who smoke. We mislead patients when we evaluate smoking cessation products under conditions that will not be experienced by the average consumer. He notes that no study has yet evaluated varenicline as a stand-alone aid. Few real-world "quitters" will receive the 25 professional counseling and support sessions that were seen in early manufacturer-supported studies with varenicline. Counseling and support have already proven their worth in smoking cessation. One can only hazard a guess as to how much of varenicline's 18.6% 1-year quit rate can be attributed to the drug and how much to counseling and support.

Despite the enormous mortality and morbidity caused by tobacco use, smoking cessation counseling skills are barely taught in medical school and residency training, if at all. Smoking cessation holds little intellectual appeal for physicians compared to most diagnostic challenges and treatment decisions, doubtless because there is little immediate observable improvement in disease outcome.

To make matters worse, TV commercials for varenicline and nicotine replacement products have created unrealistic expectations for patients and have medicalized smoking into a problem with a seemingly simple, prescribable solution.

Christakis' and Fowler's landmark analysis of Framingham Heart Study data from over 32 years of follow-up showed that those who stop smoking are far more likely to do so when they associate with others who have stopped smoking, including family members, co-workers, neighbors, friends, and friends-of-friends (N. Engl. J. Med. 2008;358:2249-58).

I believe the most important question we should now ask every patient who smokes is, "Who among your closest relatives and friends has successfully stopped smoking?"

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FDA Clears Spiriva Inhaler of Concerns About Stroke, MI

BY ELIZABETH MECHCATIE

Treatment with the Spiriva HandiHaler, which contains a dry powder formulation of the anticholinergic tiotropium, does not appear to be associated with an increased risk of stroke, myocardial infarction, or cardiovascular death in patients with chronic obstructive pulmonary disease, the Food and Drug Administration announced.

The FDA has now completed its safety review of this product "and believes the available data do not support an association between the use of Spiriva HandiHaler and an increased risk for these serious adverse events," according to an agency statement.

The Spiriva HandiHaler, marketed by Boehringer Ingelheim and Pfizer, was approved in 2004 for the long-term maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. It is administered once daily.

The FDA has been conducting a safety review of the Spiriva HandiHaler since the manufacturer submitted data suggesting that treatment with tiotropium was tied to a small increased risk of stroke compared to placebo (2 cases per 1,000 treated patients). It announced the review in March 2008. In October 2008, the agency issued a statement about two published studies that suggested an increased risk of stroke, MI, and death in patients treated with tiotropium.

The latest FDA statement said that a 4-year study comparing treatment with the Spiriva HandiHaler to placebo in almost 6,000 patients with COPD found no increase in the risk of these outcomes in the treatment arm.

The study was reviewed by the FDA's Pulmonary-Allergy Drugs Advisory Committee in November 2009. In a near unanimous vote, the panel agreed that the data adequately resolve the potential safety concerns for stroke and adverse cardiovascular outcomes associated with this product. ■

Gene Found Linked to Asthma Susceptibility

Researchers have identified a genetic locus on chromosome 1q31 that is significantly associated with susceptibility to asthma.

Two candidate genes at this locus were identified in a genome-wide association study of North American children of European ancestry, and the findings were replicated in a cohort of European adults and a population of North American children of African ancestry, said Patrick M. A. Sleiman, Ph.D., of Children's Hospital at Philadelphia's Center for Applied Genomics and his associates (N. Engl. J. Med. 2009 [doi:10.1056/NEJMoa0901867]).

The researchers first performed a genome-wide association study in a cohort of 793 children (mean age 7 years) who had moderate to severe asthma requiring daily corticosteroid therapy. A control group of 1,988 nonasthmatic children also was assessed. All the children were Americans of European ancestry.

Eight single-nucleotide polymorphisms (SNPs) were found to be significantly associated with asthma. All mapped to the DENND1B gene or the CRB1 gene at a novel locus on chromosome 1q31. The findings were replicated in a European cohort of 917 adults with childhood-onset asthma and 1,546 control subjects.

A cohort of 1,667 African American children with asthma and 2,045 African American children without asthma was then assessed. Again, each of the eight SNPs on chromosome 1q31 was strongly associated with asthma.

The study was supported by an award from the Children's Hospital of Philadelphia, and grants from the state of Pennsylvania, the Lundbeck Foundation, and the National Institutes of Health. No conflicts of interest were reported.

—Mary Ann Moon