

# New Drug Boosts Smoking Quit Rates

BY MITCHEL L. ZOLER  
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DALLAS — The first agent from a new drug class was safe and effective in helping patients stop smoking in three phase III studies that involved more than 3,000 patients.

Treatment with varenicline, a selective nicotinic acetylcholine-receptor partial agonist, led to smoking quit rates that doubled what was achieved with bupropion (Zyban, GlaxoSmithKline) and quadrupled the rate with placebo in a pair of acute therapy studies, Serena Tonstad, M.D., reported at the annual scientific sessions of the American Heart Association.

The third study showed that 24 weeks of treatment with varenicline was safe and better maintained abstinence from smoking, compared with a 12-week course of the drug.

All of the studies were sponsored by Pfizer Inc., which is developing the drug and plans to market it as Champix. The phase III data presented at the meeting were part of a new drug application submitted to the Food and Drug Administration in November, according to a statement released by Pfizer. Dr. Tonstad has received honoraria from Pfizer as a speaker and a consultant.

On the basis of the results, varenicline “was effective and appeared safe,” said Erika S. Froelicher, Ph.D., a specialist in smoking cessation and a professor of nursing and epidemiology at the University of California, San Francisco. “We can feel confident that help is on the way as we await this promising new drug,” said Dr. Froelicher, who was not involved in these studies and reported no financial relationships.

Varenicline was designed by researchers as a nonnicotine agent that is both an antagonist and partial agonist for the nicotine receptor. As an antagonist, the drug prevents nicotine from binding to its receptor, thus reducing the positive reinforcement that usually accompanies smoking and “breaking the cycle of addiction,” said Dr. Tonstad, department of preventive cardiology, Ullevål University Hospital, Oslo.

The drug’s agonist side means that it also partially activates the nicotine receptor,

which blunts withdrawal symptoms and curbs craving after patients stop smoking.

The two acute treatment studies had an identical design and were done at centers in the United States. Each study included slightly more than 1,000 people who smoked about a pack of cigarettes daily and had smoked for about 25 years. All the participants were motivated to quit.

They were randomized to treatment with 1-mg varenicline b.i.d., 150-mg bupropion b.i.d., or placebo. After receiving their assigned agents for 7 days while continuing to smoke, the participants were told to stop smoking on day 8. Treatment continued for another 11 weeks, during which they had weekly examinations and attended brief weekly motivational support sessions that focused on the behavioral aspects of cessation.



Varenicline prevents nicotine from binding to its receptor and helps break addiction, said Dr. Serena Tonstad.

Successful cessation was defined as not inhaling even a single puff of cigarette smoke during the last 4 weeks of treatment. Abstinence was monitored during weekly clinic visits by expired carbon monoxide levels.

In both studies, during weeks 9-12 of treatment, 44% of those in the varenicline group abstained from smoking, as did 30% of those in the bupropion group and 18% of those in the placebo group.

Statistical analysis calculated that the odds ratio of smoking cessation was nearly fourfold higher in the varenicline group than in placebo patients, and nearly twice as high in the varenicline group than in those receiving bupropion—the only drug approved in the United States for smoking cessation. All of the rate differences

between the varenicline and comparator groups were statistically significant.

A secondary end point for both studies was the rate of confirmed, continuous abstinence during the 44-week period starting with the ninth week of treatment and continuing to 1 year after the study’s start. (Participants were treated for the first 4 weeks and during weeks 9-12, and then were off treatment for the next 40 weeks.)

Abstinence rates during this period were about 22% for the varenicline-treated people in both studies, compared with a 16% rate in those treated with bupropion and about 9% in those who got placebo.

The third study, done in the United States and at sites in other countries, began with 1,927 people who received 1-mg varenicline b.i.d. on an open-label basis for 12 weeks. At the end of this period, 1,236

(64%) patients remained abstinent from smoking and were eligible for the maintenance phase. The second half of the study randomized 602 people to continue to receive varenicline for a second 12-week period, and 604 were randomized to placebo.

During weeks 13-24, continuous abstinence from smoking was achieved at a rate of 71% in the varenicline group and a rate of 50% in the placebo group, a statistically significant difference. From week 13 to 52, the abstinence rates were 44% in the group treated for 24 weeks, compared with a 37% in those treated for 12 weeks. The results showed that a second 12-week course of varenicline was better than placebo for helping people stay off cigarettes, said Dr. Tonstad, who is also a professor of nutrition at the University of Oslo.

In all patients, the most common adverse effect from varenicline was nausea, which overall affected about 30% of those taking the drug. In about two-thirds of people who had nausea, the effect was mild. Other reported adverse effects were headache and vivid dreams. In general, varenicline appeared safe and was well tolerated, said Dr. Tonstad, but she did not report any data on hepatic and renal function in patients taking the drug. Weight gain was similar in the varenicline and placebo groups. ■

# Early COPD Evaluations Often Lacking

BY DOUG BRUNK  
San Diego Bureau

SAN DIEGO — Primary care physicians use the nonspecific ICD-9 code 496.xx to indicate chronic obstructive pulmonary disease more frequently than specific ICD-9 codes for the disease, Vijay N. Joish, Ph.D., reported in a poster session at the 100th International Conference of the American Thoracic Society.

Most COPD diagnoses in primary care offices are being made without pulmonary function test results or any recorded history of risk factors, said Dr. Joish of the pharmacotherapy outcomes research center at the University of Utah, Salt Lake City.

The findings, part of what he said is the largest study of its kind, confirm previous studies suggesting that patients with COPD continue to be undiagnosed and undertreated. “There is an underuse of spirometry and lung function tests to diagnose COPD,” he said in an interview. “I’m not sure how physicians would get the most effective treatment if they don’t have that kind of information.”

He and his associates used GE Centricity, a national electronic medical records database containing more than 16 million patient charts, to identify adults diagnosed with COPD during or after 1990 in office-based family practice, internal medicine, and general practice settings. They identified 35,752 patients by ICD-9 codes 491.xx (bronchitis type), 492.xx (emphysema type), and 496.xx (not elsewhere specified) but studied only the 14,691 who had at least 6 months of health care resource use prior to their first diagnosis of COPD.

The investigators evaluated pulmonary function tests and diagnoses of specified risk factors in the 14,691 patients before and after the first diagnosis of COPD to determine the progression of the disease. They used the Global Initiative for Chronic Obstructive Lung Disease criteria to measure disease severity and defined risk factors as physician recorded diagnosis of smoking, bronchitis, dyspnea/shortness of breath, and cough or abnormal sputum.

Of the 14,691 patients, 10,494 (71%) had an ICD-9 diagnosis of 496, the nonspecific code to indicate COPD. Only 383 patients (less than 3%) had any pulmonary function test before or on their first day of COPD diagnosis, and 426 (less than 3%) had pulmonary function tests after diagnosis. In addition, 4,612 patients (31%) had a recorded risk factor prior to their COPD diagnosis.

In the poster, Dr. Joish and his associates acknowledged that some of the medical records used in the study might have been incomplete. “For instance,” they wrote, “handheld spirometry tests may not [have been] captured and/or appropriately transcribed electronically into the database.”

Pfizer Inc. funded the study. ■

# Even Very Light Smoking Greatly Increases Health Risks

Men and women who smoke as few as 1-4 cigarettes daily have a significantly increased risk of dying from ischemic heart disease and from all causes, according to a very large prospective study by Kjell Bjartveit, M.D., of the National Health Screening Service in Oslo, and a colleague.

Furthermore, the study, which followed 23,521 men and 19,201 women for more than 10 years, determined that women who are light smokers have an increased risk of lung cancer (Tobacco Control 2005;14:315-20).

After controlling for age, systolic blood

pressure, total serum cholesterol, serum triglycerides, physical activity, body mass index, and height, the investigators calculated that light smokers had about a 50% increased risk of dying from all causes, compared with nonsmokers—a statistically significant increase in risk.

There was a clear dose-response relationship between daily cigarette consumption and adverse health outcomes. For example, men who smoked 20-24 cigarettes daily—not light smokers—had more than three times the risk of dying from all causes than nonsmokers.

Previous studies demonstrated similar

dose-response curves, but in most, the lowest consumption group was set at 1-9 or 1-15 cigarettes daily. This allowed the Norwegian tobacco industry to suggest that there was a threshold level of smoking for which there were no health risks.

Participants in the study, who were residents of Oslo or one of three rural counties in Norway, were 35-49 years old when they were enrolled, between 1972 and 1978.

The investigators concluded that policymakers and health educators should emphasize more strongly that light smokers are endangering their health.

—Robert Finn