

# Novel Drug Boosts Smoking Cessation Rates

*Varenicline is a safe and effective treatment for breaking the smoking addiction cycle, studies find.*

BY MITCHEL L. ZOLER  
Philadelphia Bureau

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, Dr. Serena Tonstad 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 was 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 study results, varenicline “was effective and appeared safe,” commented 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,” according to Dr. Tonstad, who is with the 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



**Dr. Serena Tonstad of Ullevål University Hospital, Oslo, said smoking quit rates were nearly fourfold higher in the varenicline group than in placebo patients.**

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 smoking cessation.

Successful cessation, the primary end point of both studies, 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

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 start of the study. (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% rate 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 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. ■

## Gender Differences Observed in Beliefs of AA Participants

BY BETSY BATES  
Los Angeles Bureau

SANTA BARBARA, CALIF. — Men and women are similarly devoted to long-term participation in Alcoholics Anonymous, progressing at about equal rates through the 12 steps that define the voluntary, nonprofit program for problem drinkers.

But a study presented at the annual meeting of the Research Society on Alcoholism found intriguing gender differences in two areas of Alcoholics Anonymous (AA) participation.

Women just starting out in AA tended to place more emphasis on deferring to a higher power for their recovery than women who had spent more than a year in the program.

For men, the pattern was reversed. Men just starting out were much less likely than women to place a high degree of importance on a higher power’s role in their recovery. But those who had spent more than a year in the program attributed a great deal of importance to a higher power’s role, surpassing women’s ratings on this measure.

Men, regardless of how long they had participated in AA, were significantly more likely than women to participate in sister AA 12-step programs such as Narcotics Anonymous.

J. Scott Tonigan, Ph.D., of the center on alcoholism, substance abuse, and addictions at the University of New Mexico, Albuquerque, studied the responses of 99 AA members from five AA groups to a series of questionnaires about the program.

The cohort included 73 men and 26 women. Their average age was 44, and they reported an average of 69 months of abstinence.

Most had attended AA for more than 1 year, but 35 were newcomers, allowing Dr. Tonigan to capture differences in participants’ outlooks based on their longevity in AA.

Regardless of gender, participants who had spent more time in the program were significantly more likely to say they were following the central constructs of AA: making amends to others, believing in a higher power, practicing AA behaviors, and completing steps in the program.

“Perhaps... they had more time to do so relative to the short-term AA members,” Dr. Tonigan wrote in his poster.

In this study, just 3 of 26 women but 28 of 73 men said they had attended sister AA programs. Women who had been involved with AA longer placed less emphasis on a higher power than did women who had just started AA, while for men the reverse was true.

Dr. Tonigan said it is possible that these unexpected findings could be attributable to the cross-sectional nature of the study, to gender differences in substance abuse (with regard to attendance at sister AA program meetings), or to type 1 error, because the number of subjects in the study was small.

He stressed that men and women tend to similarly complete AA steps, read AA literature, and find sponsors—all key elements in the program’s proven ability to foster abstinence.

However, he said, a better understanding of what keeps men and women attending AA may help clinicians to assist their patients in benefitting from the mutual-help group. ■