Extended Varenicline Aids Slow-to-Quit Smokers

BY BRUCE JANCIN
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MUNICH — Smokers who struggle to quit during the standard 12-week course of varenicline derive particular benefit from a second 12-week stint on the drug, a large international clinical trial has shown.

In contrast, the study demonstrated, the majority of early quitters—that is, patients who gave up smoking during their first week on varenicline and stayed off cigarettes for the remainder of the 12 weeks—were still abstinent a year later, whether they received a second 12 weeks of varenicline or placebo, Dr. Serena Tonstad reported at the annual congress of the European Society of Cardiology.

These findings can aid physicians in making the most efficient use of varenicline, marketed as Chantix in the United States and Champix elsewhere, added Dr. Tonstad of the University of Oslo.

She reported on 1,208 smokers who were abstinent for at least the last week of a 12-week course of varenicline and then were randomized and double blinded to a further 12 weeks of the nicotinic acetylcholine receptor partial agonist or to placebo.

Patients who had their last cigarette by the target quit date—the end of week 1 of the initial 12 weeks of varenicline—had a 55% smoking cessation success rate at 1 year. Patients who took longer to quit during the initial 12 weeks had a much greater risk of relapsing within a year. For example, those who had their last cigarette at week 11 had a 5.6% abstinence rate at 1 year—just 1/10 of the success rate of the early quitters.

The encouraging news from this study is that late quitters who received 12 more weeks of varenicline had a significantly increased likelihood of still being smoke free 52 weeks after their first attempt to give up the habit. Indeed, 35% of late quitters who took varenicline for 24 weeks were continuously abstinent at the 1-year follow-up mark, compared with just 23% of those who received 12 weeks of placebo after their 12 weeks of varenicline.

The clinical implication is that physicians ought to seriously consider preferentially offering a second 12 weeks of varenicline to smokers who have frequent relapses or a delayed quit attempt during the usual 12-week course of the drug, according to Dr. Tonstad.

In a separate but complementary presentation, Dr. David Gonzales of Oregon Health and Science University, Portland, argued that quitting smoking with the assistance of varenicline is a more dynamic process than previously thought.

He pooled data from two identical phase III U.S. double-blind clinical trials totalling 2,052 smokers randomized to 12 weeks of varenicline, sustained-release bupropion, or placebo.

Their mean age was 43 years, with a 25-year smoking history. At enrollment they averaged more than 21 cigarettes per day. Overall, 85% of subjects had made one or more prior unsuccessful attempts to quit.

The principal results of the two studies—varenicline-treated patients had a significantly higher smoking cessation rate than those on bupropion SR or placebo—have been published (JAMA 2006;296:47-55, 56-63).

The new secondary findings presented by Dr. Gonzales addressed differential patterns of quitting during the treatment period and rates of posttreatment relapse. Of the varenicline group, 24% were immediate quitters who stopped smoking in the first week and remained continuously abstinent through week 12, compared with 18% on bupropion SR and 10% on placebo.

But varenicline also resulted in a higher delayed quit rate. Indeed, 44% of the varenicline group achieved continuous abstinence in weeks 9-12, compared with 30% on bupropion SR and 18% on placebo. And nearly half of varenicline-treated patients who remained continuously abstinent during that period were delayed quitters who became abstinent only at that point; that's a higher proportion of late quitters than in the other treatment arms, Dr. Gonzales explained.

After the 12 weeks of active treatment, relapses steadily increased at the same rate for each treatment group.

In February, the Food and Drug Administration issued an alert that highlighted additional warnings regarding the possibility of serious neuropsychiatric symptoms the possibility in varenicline-treated patients.

Those symptoms included agitation, depressed mood, and suicidality (www.fda.gov/CDER/Drug/infopage/varenicline).

Dr. Gonzales presented a summary of the psychiatric symptoms occurring in the two trials. The frequency was relatively low, and generally similar in the varenicline and bupropion SR groups. Two notable exceptions were the higher rates of abnormal dreaming with varenicline and of insomnia with bupropion SR (see chart).

The studies reported by Dr. Gonzales and Dr. Tonstad were funded by Pfizer Inc. Both investigators are consultants to the company. Dr. Gonzales disclosed ownership of five shares of Pfizer stock. ■

Prevalence of Psychiatric Symptoms in Varenicline Trials

	Varenicline	Bupropion SR	Placebo
Depression	1.4%	1.5%	1.0%
Depressed mood	1.0%	0.9%	0.4%
Agitation	0.7%	1.5%	0.9%
Anxiety	3.5%	4.6%	3.9%
Sleep disorder	5.2%	5.4%	3.2%
Insomnia	13.9%	21.4%	12.3%
Abnormal dreams	11.7%	5.7%	4.5%

Source: Dr. Gonzales

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