Methadone Dose Higher With Chronic Pain

**BY DEEANNA FRANKLIN**

**Associate Editor**

**O RLANDO , F LA . — Varenicline, a first-of-its-kind selective nicotinic receptor partial agonist, has racked up unprecedented smoking-cessation success rates in a pair of phase II clinical trials, Cheryl A. Oncken, M.D., reported at the annual meeting of the American College of Cardiology. Based on these extremely encouraging albeit short-term results, multiple year-long phase III trials are underway using varenicline at 1.0 mg twice daily, a Pfizer spokesman told this newspaper. The two phase II placebo-controlled studies totaled 1,253 smokers. In one 6-week study, 48% of participants assigned to 1.0 mg of varenicline twice daily quit smoking for a 28-day period as determined by review of daily smoking diaries, compared with 37% on 1.0 mg/day of the drug, 33% on 150 mg of bupropion twice daily, 29% on 0.5 mg/day of varenicline, and 17% on placebo, said Dr. Oncken of the University of Connecticut, Farmington.

In the other study, which lasted 12 weeks, 51% of patients on 1.0 mg of varenicline twice daily abstained from smoking during weeks 9-12 as confirmed by carbon monoxide testing. This was also the case for 45% of those randomized to 0.5 mg of the drug twice daily and for 12% of the placebo group. The adjusted odds ratios for abstinence were 6.1 and 7.8 for 0.5 and 1.0 mg of varenicline twice daily, respectively, compared with placebo.

The most common varenicline-related side effect was transient mild to moderate nausea. Tolerability compared favorably with placebo in both studies. It also compared favorably with bupropion—a drug with a Food and Drug Administration indication for smoking cessation—in the one comparative trial where it was used, with discontinuation due to adverse events occurring in 11% of patients in the high-dose varenicline group and 16% of those on bupropion. No varenicline-related safety issues arose during monitoring of laboratory tests and ECGs.

Nicotine dependence in smokers is mediated via the neuronal α4β2 nicotinic receptor. Varenicline is believed to act by blocking nicotine binding to the receptor and interfering with smoking’s extremely potent reinforcement and reward effects. Moreover, partial activation of the α4β2 receptor by varenicline during abstinence has been hypothesized to relieve nicotine craving and withdrawal symptoms, Dr. Oncken explained.

Her studies were sponsored by Pfizer Global Research and Development.

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Data Watch

**Nonmedical Use of Stimulants Is Highest Among Whites, Native Americans**

**BY DIANA MAHONEY**

**New England Bureau**

**BOSTON — Children who experiment with smoking even minimally before age 11 are more likely to take up smoking as teens than are their nonexposed peers, Jennifer Fidler reported at the annual meeting of the Society of Behavioral Medicine. Because there is an apparent protracted period of dormant vulnerability—or sleeper effect—before social or environmental conditions trigger the onset of a stable smoking pattern, ‘interventions should target the prevention of first, short experimentation with smoking,’ she said.**

Using data from the 5-year longitudinal Health and Behavior in Teenagers Study (HABITS) of 5,000 British adolescents, which included yearly assessments of smoking status, Ms. Fidler and her colleagues at University College London calculated the probability of becoming a smoker as a function of having tried smoking just once by age 11.

Early one-time triers were significantly more likely than those who had never smoked at age 11-12 to take up current smoking for the first time up to 3 years later. The study data showed that very few participants reported current smoking at age 11-12, ‘making this an ideal time to study smoking progression,’ she said.

After the investigators controlled for personal factors known to influence smoking—including ethnicity, socioeconomic deprivation, gender, family/peer smoking, and conduct problems—logistic regression analyses confirmed a statistically significant sleeper effect, Ms. Fidler said. The adjusted odds for taking up smoking at 1, 2, and 3 years following initial exposure relative to same-age nonexposed peers were 6.3, 2.9, and 2.1, respectively.

‘Only after 4 years of nonsmoking following an initial try before age 11 was the difference between triers and nontriers not significant,’ she said.

Various behavioral and biophysical conditions may contribute to the sleeper effect, including the possibility ‘that early nicotine exposure alters neurologic reward pathways,’ Ms. Fidler said. ‘Or it may be that the first smoking experience breaks down such barriers to smoking as fear and insecurity about how to smoke, or that personality traits leading to the initial try may continue to stand individuals at an increased risk.’

From a policy perspective, the findings suggest that early interventions should be aimed at preventing early experimentation with smoking to reduce the risk of smoking uptake, Ms. Fidler said. Additionally, ‘interventions should target adolescents who report having tried smoking, albeit just once, because of their increased risk of later smoking.’

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Experimentation Before Age 11 Predicts Later Smoking Habits

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**ADDITIONAL CONTENT**

**Smoking Cessation Drug Could Be Major Advance**

**BY BRUCE JANCIN**

**Denver Bureau**

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