Vaccine May Help Some Heavy Smokers Quit

BY JANE SALODOF MACNEIL
Southwest Bureau

ORLANDO — Swiss researchers have reported that a vaccine against nicotine addiction helped a subgroup of long-term, heavy smokers kick the habit.

The CYT002-NicQb vaccine did not perform significantly better than placebo in intent-to-treat data from a phase II clinical trial that enrolled 341 healthy smokers aged 18-70 years. Six-month results showed that 64 (40%) of 159 smokers given the vaccine and 25 (31%) of 80 smokers in the control group were able to abstain from cigarettes for 8-24 weeks.

An advantage emerged, however, when the researchers subdivided the vaccine cohort into thirds based on titers of antibodies against nicotine. Among smokers who had a high antibody response, 30 (57%) of 53 were able to quit smoking. But in both the low- and medium-antibody-response subgroups, just 17 (32%) of 53 smokers stayed off cigarettes.

"The difference between the placebo and high-response groups was highly significant," principal investigator Jacques Cornuz, M.D., said at the annual meeting of the American Society of Clinical Oncology. "These data clearly suggest antibodies against nicotine are effective in helping people to quit smoking."

The high-antibody-response group also showed an advantage among participants who cut back on smoking but did not succeed at giving up cigarettes completely, according to Dr. Cornuz of the Centre Hospitalier Universitaire Vaudois Lausanne (Switzerland). They smoked fewer cigarettes per day than the other subgroups. The response duration beyond 50 days has not been established.

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In interviews after the presentation, executives from the trial's sponsor, Cytos Biotechnology of Zurich, said they plan to include a greater number of smokers who have a high response to CYT002-NicQb in a phase III trial scheduled for 2007. The company has announced its goal to bring the vaccine to market by the end of 2009.

A spin-off from the Swiss Federal Institute of Technology, Cytos is also working on vaccines against obesity, hypertension, arthritis, psoriasis, and other chronic conditions.

Cytos president/CEO Wolfgang A. Renner and Philipp Müller, M.D., executive vice president for clinical development and regulatory affairs, said the nicotine vaccine is the most advanced among their 27 vaccine candidates for various conditions, 6 of which they described as being in development.

Dr. Cornuz and his colleagues conducted the phase II study at three centers in Switzerland. In his presentation, he said the vaccine is designed to give nicotine "the look of a virus" by coupling nicotine to a viruslike particle. The resulting antibody response interferes with the rewards of nicotine addiction by reducing the amount of nicotine entering the brain and the rate at which it enters.

The researchers enrolled people who had smoked 10-40 cigarettes a day for 3 or more years and had a Fagerström Test for Nicotine Dependence score of 5 points or more. In the vaccine and placebo groups, median values at baseline for subject characteristics were 42 years of age, 25 cigarettes smoked daily, 25 years of smoking, and a Fagerström score of 7. Both groups had a median of three failed attempts.

People with significant somatic or psychiatric diseases were excluded, as was anyone who had used any kind of smoking cessation therapy during the previous 6 months. All patients in the study received smoking cessation counseling along with five monthly doses of vaccine or placebo.

Outcomes were self-reported and were verified by carbon monoxide testing at monthly visits. Participants entered the study with median carbon monoxide concentrations in exhaled air of 29 parts per million (ppm) in the vaccine group and 27 ppm in the placebo group. The threshold for abstinence was less than 10 ppm.

Dr. Cornuz reported that adverse events were common but similar overall to the severity of such events with placebo. Of the vaccine group, 68% had mild effects, 28% reported moderate effects, and 4% had severe effects.

The most frequent effects of the vaccine were flu-like symptoms after injection in nearly 70% of subjects and pyrexia and headache in about 40% each. Other common effects included nasopharyngitis (in about 30%), injection-site pain (in about 20%), and rigors and myalgia (both in about 10%). The side effects analysis was based on the 341 participants. Results excluded 44 people who used a nicotine replacement therapy and 57 for whom antibody data were incomplete. ■

Fewer Than Half of OxyContin Prescriptions Taken as Directed

BY BETSY BATES
Los Angeles Bureau

PALM SPRINGS, CALIF. — Just 45% of prescriptions for the opiate OxyContin (oxycodone HCl controlled release) are taken as directed by patients being treated for nonmalignant pain, according to a study of urine samples from approximately 5% of the nation's outpatient pain clinics.

Fully 40% of the drug was recycled among other patients being treated for pain in 264 clinics whose combined caseloads exceeded 33,000 patients, Michael Kell, M.D., of the Labyrinth Institute of Smyrna, Ga., reported at the annual meeting of the American Academy of Pain Medicine.

Another 15% of OxyContin prescriptions were diverted to the black market, said Dr. Kell, who was chosen to present his poster in an oral format at the meeting.

Dr. Kell, a toxicologist, collected his data using software technology that interprets highly specific urinalysis results that control for urine concentration and acidity and patient BMI.

The urine from 55% of approximately 11,000 patients prescribed OxyContin either contained more of the drug, or less, than what would be expected based on the amount prescribed. To allow for time of day and other variations, Dr. Kell considered a patient compliant if the level of OxyContin in his or her urine was within three standard deviations of the mean.

Interestingly, about 15% of patients prescribed OxyContin had none of the drug in their urine. At the same time, many patients being treated with other pain drugs in the clinics had OxyContin in their urine, suggesting that "most of the diversion was patient to patient," Dr. Kell said.

Funding for Dr. Kell's study was provided by UD Testing Inc., a Marco Island, Fla., company that uses Dr. Kell's software to monitor patient compliance with prescription medicine.

Another study presented at the meeting described very preliminary results from a novel oxycodone drug formulation called Remoxy. The formulation delivers a long-acting dose of the opiate in a gel cap designed to be impervious to efforts to extract the full dose to achieve a "spike" effect by crushing, freezing, heating, or dissolving it in various substances. Current formulations of the drug can be manipulated in this way, adding to abuse and diversion.

Plasma concentrations were markedly lower in 20 subjects who took Remoxy after it had been tampered with, compared with concentrations among people who had taken crushed controlled-release formulations of oxycodone.

The industry-designed study was funded by Pain Therapeutics Inc. of San Francisco. ■