Drug Implants Help Reduce Opioid Dependence

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Buprenorphine implants helped approximately 40% of patients addicted to opioids markedly reduce their drug use for 6 months in a phase III study of this new method of delivery.

In addition, two-thirds of the study subjects who received the implants completed 24 weeks of treatment without experiencing cravings or withdrawal symptoms compelling them to drop out, said Dr. Walter Ling of the UCLA Integrated Substance Abuse Programs, Los Angeles, and his associates.

In comparison, studies of sublingual buprenorphine found a median adherence of only 40 days in clinical settings, and 6-month clinical trials report subject retention rates of 35%-38%, the investigators noted.

The implantable formulation of buprenorphine was developed to address dependent patients' problems with adherence and "diversion," or using the drug for some purpose other than treatment, such as selling it. The implants deliver an initial pulse of buprenorphine followed by the release of a constant, low level for 6 months.

Dr. Ling and his colleagues performed their industry-sponsored phase III study at 18 community addiction treatment centers across the United States. In all, 108 subjects were randomly assigned to receive four buprenorphine implants and 55 to receive four placebo implants in the subdermal space in the inner side of the nondominant arm.

The study subjects were allowed to receive supplemental sublingual buprenorphine-plus-naloxone tablets if they experienced significant withdrawal

FDA Okays Long-Acting Naltrexone

The injectable extended-release formulation of naltrexone, marketed as Vivitrol, has been approved as a treatment for preventing relapses in people who have undergone opioid detoxification, the Food and Drug Administration announced.

Vivitrol, which was approved in 2006 for the treatment of alcohol dependence, is administered in an intramuscular injection once a month, in patients who have no opioids remaining in their system.

If opioids are present, patients may experience withdrawal symptoms, according to the FDA statement. Naltrexone is an opioid antagonist.

Approval was based on the results of a 6-month study of 250 patients who were completing or had recently completed detoxification and were no longer physically dependent on opioids.

Between the 5th week and the end of the study, 36% of those treated with Vivitrol (one 380-mg injection once a month) had not used opioids at all, compared with 23% of those on placebo, a significant difference. All patients received psychosocial support during the study.

Side effects associated with Vivitrol treatment include nausea, fatigue, headache, dizziness, vomiting, reduced appetite, painful joints, and muscle cramps, the FDA statement said.

Serious side effects include injection site reactions, allergic reactions, hepatotoxicity, and depression, as well as suicide and suicidal thoughts and behavior.

Customized needles provided in the Vivitrol package must be used to inject the medication as an intramuscular gluteal injection, according to the FDA and Alkermes Inc., the manufacturer of Vivitrol.

The FDA has asked the company to conduct postmarketing pharmacokinetic and efficacy studies of Vivitrol in patients aged 12-16 years.

Serious adverse reactions associated with Vivitrol should be reported to the FDA's MedWatch program at 800-332-1088 or www.fda.gov/medwatch.

–Elizabeth Mechcatie

VITALS

Major Finding: Among patients addicted to opioids, 40% were able to discontinue illicit drug use for 4 months and 37% for 6 months after receiving buprenorphine implants, while only 28% and 22%, respectively, discontinued illicit drug use after receiving placebo implants.

Data Source: A phase III, randomized placebo-controlled trial of 163 patients treated at 18 U.S. clinical centers and followed for 6 months.

Disclosures: This study was funded by Titan Pharmaceuticals, maker of the buprenorphine implants, which was involved in the design and management of the study, data collection and analysis, and preparation and approval of the manuscript. Dr. Ling and his associates reported numerous ties to drug and device manufacturers.

symptoms or cravings. They also were allowed to get one additional implant if necessary. All also received individual drug counseling twice a week for 3 months and weekly thereafter.

The patients' use of illicit drugs was monitored throughout the study by urinalyses done 3 times per week.

The primary outcome was early treatment response, assessed as the percentage of the 48 urine samples obtained during the first 16 weeks of the trial that were negative for illicit opioids. This rate was 40% with the buprenorphine implants, vs. 28% with the placebo implants, the researchers said (JAMA 2010;304:1576-83).

For the full 6-month treatment period, in which 72 urine samples were analyzed for each subject, 37% were negative for illicit opioids in the buprenorphine group, compared with 22% for placebo.

Treatment adherence was significantly better with the active treatment at 16 weeks (82% with buprenorphine vs. 51% with placebo) and at the conclusion of the study (66% vs. 31%). Throughout the study, the implant group also had significantly lower scores on measures of opiate withdrawal and opioid craving. No patients who received buprenorphine implants were classified as treatment failures, while 31% who received placebo implants were. ■