New Smallpox Vaccine Backed for High-Risk Needs

BY ELIZABETH MECHCATIE Senior Writer

GREATBERSBURG, MD. — A more modern version of the smallpox vaccine appears to be safe and effective enough to use “where it is determined that there is a high risk of exposure to smallpox virus,” according to a Food and Drug Administration advisory panel.

At a meeting, members of the FDA’s Vaccines and Related Biological Products Advisory Committee agreed that the ACAM2000 vaccine should be submitted to postmarketing studies that follow people who developed vaccine-associated myoecarditis and determine risk factors for myocarditis.

The vaccine, which is derived from Dryvax, the currently licensed smallpox vaccine, is not being considered for use in the general population. Panelists emphasized the nature of the situations in which the risk-benefit profile of ACAM2000 would be considered favorable.

“This and Dryvax are the least-safe vaccines that we will have licensed in this country, and we have to weigh that against the risk of smallpox,” said the panel chair, Dr. Ruth A. Karron, professor in the department of international health at Johns Hopkins University, Baltimore.

The rate of myocarditis—one in about every 150 vaccine recipients—was “far and above” any serious adverse event of that magnitude associated with other vaccines, emphasized Dr. Jack Stapleton, professor and director of infectious diseases at the University of Iowa, Iowa City.

If this were a vaccine being considered for routine use in the general population, the risk of myocarditis seen in clinical trials “would be unacceptable,” added Dr. Mon- ica Farley, professor of medicine at Emory University, Atlanta.

Some other well-documented complications of smallpox vaccination that date back to the era of routine smallpox vaccine include generalized vaccinia, eczema vaccinatum, postvaccinial encephalitis, inadvertent inoculation, fetal vaccinum, and death.

The panel was not asked to vote specifically on whether to approve the vaccine. The FDA typically follows the advice of its advisory panels, although that advice is not binding.

If approved by the FDA, the vaccine would not be made available commercially. Instead, it would be used for the national vaccine stockpile and for military personnel deployed to areas of the world where the threat of exposure to smallpox as a biologic weapon is considered high. Acambis Inc. manufactures the vaccine, which was developed under a contract with the Centers for Disease Control and Prevention for stockpiling purposes.

In fact, Acambis has already supplied 192.5 million doses to the U.S. Strategic National Stockpile, according to the company. There is a limited supply of Dryvax remaining, which is itself reserved for the military and laborato- ryr workers.

The derivation of ACAM2000 from Dryvax uses modern cell culture techniques without animal serum, and is grown in a continuous cell line.

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In a second study of people aged 11-84 years who had been vaccinated against smallpox, however, the take rate was 84% among those who received ACAM2000, compared with 98% of those who re- ceived Dryvax.

The majority of side effects were inoculation site reactions and systemic symp- toms, including fever, rash, lymph node pain, headache, fatigue, and myalgia.

In both studies, participants were closely monitored for myocarditis, which was diagnosed in 10 naive recipients (7 of whom were in the ACAM2000 treatment group). The myocarditis cases occurred at a mean of 11 days after receiving the vaccine and resolved in all but one case, ac- cording to Acambis.

In the study of people without prior vaccination, the rate of myocarditis was about one case per 145 vaccinations, which is higher than the rate under the FDA. That study’s myocarditis rate was greater than the military’s rate, which a Department of Defense official at the meeting said had been one case per 6,000 primary vaccinations.

If the vaccine is approved, Acambis would launch a Risk Minimization Action Plan (RiskMAP). That would include edu- cation of vaccinees and health care providers, expedited reporting of serious adverse events, and phase IV studies to assess the vaccine’s safety profile, long-term outcomes, and myocarditis risk factors.

Role of Flu Vaccination in Reducing Health Care Utilization Is Elusive

BY MIRIAM E. TUCKER Senior Writer

BALTIMORE — In settings with good access to care and high immunization rates, ask- ing patients whether they’ve received a tetanus booster in the last 10 years is a fairly ac- curate way to determine if they need one, Dr. M. Hassan Murad and his associates said in a poster presentation at a conference on vaccine re- search sponsored by the Na- tional Foundation for Infe- cious Diseases.

Patients who answer “yes” are probably right and do not need readministration of the vaccine. But those who say ei- ther “no” or “I don’t know” should receive a tetanus diph- theria (Td) booster as long as there are no contraindications, said Murad, chief of the preven- tive medicine division of the Mayo Clinic, Rochester, Minn.

Although previous studies have demonstrated poor ac- curacy of patients’ recall of their last Td booster, this has not been evaluated previous- ly in settings where immu- nization rates are high and good documentation is avail- able. In this study, 572 pa- tients of an employee health clinic of a large health care organization were asked whether they had a Td boost- er in the last 10 years. Of those, 65.6% were able to an- swer either “yes” or “no.”

Comparison of their re- sponses with their charts yielded high sensitivity (92.4%) and low specificity (26.5%). Accuracy of recall did not differ by age or gender, Dr. Murad and his associates reported.

Their results from this study suggest patient population are likely generalizable to those of other- wise working-age adults of sim- ilar education level. “Since the results rely in significant part on human memory of a rare event—a once-every-10- years event—we do not pre- dict useful information,” Murad said.

The general characteristics of our population are they were mostly working age, educa- tional generally high school graduate or greater, and near- ly all have good access to rou- tine office care. “That is prob- ably a little more similar to many [U.S.] office practices,” Dr. Murad said in a follow-up interview.

—Miriam E. Tucker

Some Patients’ Memory Can Be Trusted on Tetanus Shots

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