NIAID Investment in a Next Generation Vaccine for Smallpox

Background

The terrorist attacks of 2001 highlighted the need for effective medical countermeasures against potential agents of bioterrorism. Smallpox, caused by the variola virus, has devastated populations for centuries. The smallpox mortality rate is more than 30 percent, and it has been estimated that throughout recorded history more people have died of smallpox than from all other infectious diseases combined. Fortunately, a vaccine was developed that, when coupled with a global vaccination policy, led to the eradication of smallpox in 1979. Although the vaccine used to eradicate smallpox was highly efficacious, it was also associated with local or systemic reactions in the majority of recipients. Because of this, once smallpox was eradicated, most of the world discontinued routine smallpox vaccination in the 1970s.

Current Smallpox Vaccine

The smallpox vaccine currently in use, Dryvax®, is highly effective, but is associated with significant reactions in more than 90 percent of vaccinees. In addition, Dryvax should not be given to individuals who are immunocompromised, such as those with HIV or those who have received organ transplants, as they are at increased risk for even more serious side effects. This leaves a significant portion of the U.S. population without access to a smallpox vaccine.

A Better Smallpox Vaccine

The National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), is funding the development of a next generation smallpox vaccine candidate, the modified vaccinia Ankara (MVA) smallpox vaccine, to help ensure that safe and effective vaccines are available for the entire U.S. population, including immunocompromised individuals. Previous NIAID research has demonstrated that MVA is nearly as effective as Dryvax at protecting monkeys against monkeypox, which is used to test the effectiveness of a smallpox vaccine because of its similarity to the smallpox virus (www.niaid.nih.gov/news/newsreleases/2004/mvavac.htm).

The MVA vaccine contains a highly weakened form of the vaccinia virus that cannot replicate in humans, and therefore is likely to be safe in individuals who currently should not receive Dryvax. Through contracts awarded by NIAID in 2003 to Bavarian Nordic A/S (Copenhagen, Denmark) and Acambis Inc. (Cambridge, Massachusetts), researchers successfully performed small-scale manufacturing of the MVA vaccines and conducted small Phase I clinical trials in healthy volunteers (www.niaid.nih.gov/news/newsreleases/2003/smallpoxvacc.htm). These early development studies showed that MVA could be manufactured in compliance with current laws and regulations, and that it was safe and was able to stimulate an immune response in healthy volunteers.

Following these successes, NIAID made new contract awards in 2004 to Bavarian Nordic A/S and Acambis Inc. to continue advanced development of their MVA candidate vaccines (www.niaid.nih.gov/news/newsreleases/2004/biod.htm). Large-scale manufacturing of the vaccines was subsequently performed. Several Phase II clinical studies are now either under way or planned, in healthy individuals and in special populations. The purpose of these studies is to further assess the safety of the vaccines, and also to begin to assess how effective the vaccines will be based on the immune responses generated.

For more information about clinical trials, visit www.clinicaltrials.gov.