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A New Vaccine to Prevent Herpes Zoster

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About 50% of persons will develop herpes zoster if they live to age 85 and the incidence of zoster is increasing. While the disease may be mild in healthy young adults, persons over age 50 and immunocompromised patients are more likely to develop complications, including zoster ophthalmicus and postherpetic neuralgia (PHN).

The live attenuated zoster vaccine licensed in the US reduces the incidence of herpes zoster by 70% in persons aged 50–59, 64% in those aged 60–69, and 38% in persons aged 70 or older.[1,2] The vaccine also reduces the incidence of PHN by 66% in persons aged 60–69 and by 67% in those aged 70 or above. The only frequent side effects have been injection site reactions.

In this issue of the *Journal*, Lal et al. report the results of a phase 3 trial of a zoster subunit vaccine consisting of a single viral glycoprotein in ASO1B Adjuvant System.[3] The vaccine was tested in nonimmunocompromised persons aged 50 or older and had a remarkable 97.2% efficacy to prevent zoster. Unlike the live attenuated zoster vaccine, the efficacy of the zoster subunit vaccine to reduce zoster did not diminish with increasing age of the subjects. The efficacy was 96.6% in the subjects 50–59 years old, 97.4% in those 60–69 years old, and 97.9% in those ≥70 years of age. The zoster subunit vaccine is a two dose vaccine while the live attenuated vaccine is a single dose vaccine.

The zoster subunit vaccine was adjuvanted with AS01B which is currently not a licensed adjuvant. This adjuvant consists of monophosphoryl lipid A and QS21, a saponin compound, formulated with liposomes. The adjuvant activates antigen-specific CD4 T cells and antibody.[4] Cell-mediated immunity, especially CD4 T cells, targeting VZV is the correlate of protection from zoster,[5] while antibody protects against varicella.[6] AS01B has been used in trials of malaria, hepatitis B, HIV, and tuberculosis vaccines.[4]

In the current study the rate of solicited systemic adverse reactions was 2.2-fold higher in the vaccine group than the placebo group (66% vs. 30%),[3] while in the live attenuated vaccine study the rate of systemic adverse events was similar (25% in vaccine recipients vs. 24% in controls).[1] In the present study 17% of the subunit vaccine recipients reported grade 3 symptoms that prevented normal activities, compared with 3.2% in the placebo group. While many of these symptoms were related to injection site reactions, grade 3 systemic reactions occurred in 11% of the vaccine recipients and 2.4% of the placebo recipients and lasted a median of 1 day. The rate of serious adverse reactions and potential immune-mediated diseases, however, was similar in both groups. Since autoimmune diseases are more

common in the elderly, it will be important to follow patients receiving this adjuvanted vaccine.

What might be the advantages of the zoster subunit vaccine? The zoster subunit vaccine might be more effective than the live attenuated vaccine. A trial is underway comparing these two vaccines for efficacy and safety (ClinicalTrials.gov, NCT02114333). The current live attenuated vaccine is contraindicated in persons with impaired cellular immunity who are at highest risk for developing zoster, such as patients undergoing hematopoietic cell transplant, persons with HIV and CD4 cell counts ≤200 mm^2, and persons receiving high doses of immunosuppressive medications. Since the zoster subunit vaccine cannot replicate it will likely be safer in these persons, although it is unclear if they will be able to mount a sufficient immune response to the vaccine. A phase 1/2 trial of the subunit vaccine in autologous hematopoietic-cell transplant recipients showed that the subunit vaccine induced VZV-specific CD4 T cells that persisted up to one year.[7] A heat-inactivated live attenuated varicella-zoster vaccine reduced the incidence of zoster in adult autologous hematopoietic cell transplant recipients.[8]

A major reason for using a zoster vaccine is to reduce complications associated with the disease, and the elderly have the highest burden of PHN and hospitalizations for zoster.[9] A study of the zoster subunit vaccine in persons aged ≥70 (ClinicalTrials.gov, NCT01165229) was initiated at the same time as the study by Lal et al. and should help to determine if the vaccine prevents PHN and other complications of zoster in the elderly where the vaccine is needed most.

The duration of the effectiveness of the vaccine will determine the need for booster doses. The live attenuated zoster vaccine significantly reduces the burden of illness due to zoster for 10 years after vaccination, but significantly reduces the incidence of zoster for only 8 years.[10] The mean follow-up in the zoster subunit vaccine study was 3.2 years; thus, it will be important to determine the duration its effect. The results of zoster subunit zoster vaccine are promising and may provide an important addition to vaccination of an aging population.

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