Waning Efficacy of the Herpes Zoster Vaccine

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(See the Major Article by Morrison et al on pages 900–9.)

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In this issue of Clinical Infectious Diseases, Morrison and colleagues report the waning efficacy of the herpes zoster (HZ) vaccine with long-term follow-up [1]. This report is the third that defines efficacy of vaccination. The first clinical trial reported the unequivocal efficacy of vaccination of individuals >60 years of age for burden of illness (BOI), incidence of postherpetic neuralgia (PHN), and incidence of HZ [2]. These 3 endpoints were assessed through 4 years postvaccination. A subsequent follow-up study were assessed through 7 years of postvaccination evaluation noted persistence of efficacy with slightly lower evidence of benefit than the original clinical trial [3], albeit not statistically significant. With the report of Morrison et al, we are able to reasonably estimate the efficacy of vaccination through year 10, and to a significantly lesser extent year 11. For BOI, the rate of decline was from 61.1% at year 4 to 50.1% in year 7 and 35.4% in year 11. The authors conclude that the efficacy for BOI, the primary endpoint of the original study, remained through year 10, but the incidence of HZ remained significant through year 8.

Several points warrant revisiting. First, and most important, the current report represents the most complete database available for the evaluation of the efficacy of the HZ vaccine in older individuals. The rigor of the original clinical trial [2] has been maintained through the long-term follow-up in the current report. Although the absence of a comparator placebo population makes definition of true outcome rates difficult, ethically, it was mandatory to vaccinate the original cohort of placebo recipients. The follow-up of this cohort of patients provides the truly unique opportunity to assess efficacy over time. The investigators as well as the volunteers should be congratulated for their continued dedication and commitment to the study.

Second, the licensure of the HZ vaccine has provided significant medical and public health value. Real-world use of the vaccine has provided both a cost-benefit and ethically, it was mandatory to vaccinate the original cohort of placebo recipients. The follow-up of this cohort of patients provides the truly unique opportunity to assess efficacy over time. The investigators as well as the volunteers should be congratulated for their continued dedication and commitment to the study.

Third, the evidence for waning efficacy is not insignificant. The percentages cited above, including the reduction from the original observation in the Shingles Prevention Study, will require rethinking public health recommendations for the deployment of this vaccine on at least a second occasion, specifically reimmunization approximately 8 years after first dose. In the absence of placebo recipients, it might be argued that the efficacy is indeed greater than that reported. Nevertheless, it raises the question as to whether or not a second vaccination will be required to maintain a high degree of efficacy in the population. It should be noted that while the vaccine is licensed for administration for individuals >50 years of age, the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices has maintained that it should be reserved for those aged >60 years due to the concern for waning immunity.

With a recommendation for a second dose of vaccine, invariably the cost-benefit analysis of such an intervention would have to be considered by public health officials. In those deliberations, evidence of toxicity, particularly cardiac events, would not limit the second dose of vaccine. Toward this end, as noted by the authors, a better understanding of host immune response to varicella zoster virus in elderly individuals is indicated.

The authors note that the findings support the need for future adequately powered and controlled prospective studies to assess long-term protection against HZ. Although this is ideal, it is highly unlikely...
that such a study will ever be duplicated to the extent that it has with even the current dataset. In any case, the authors should be congratulated for pursuing further evaluation of the effect of the zoster vaccine in older individuals.

**Note**

*Potential conflict of interest.* The author has received personal fees (outside the submitted work) as a member of the Gilead Sciences Board of Directors; as an Associate Editor for Journal of Infectious Diseases, and as a member of the GlaxoSmithKline Data Safety and Monitoring Board for a Zoster Vaccine study.

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**References**