Unsettled Issues of Zostavax Vaccine

TO THE EDITOR—The article by Schmader et al. [1] summarizing a Zostavax trial in 50- to 59-year-old participants raises new concerns and rekindles others [2]. Zostavax vaccine introduces a new virus which, like chickenpox, becomes latent in cranial nerves and autonomic and dorsal root ganglia [3]. These 2 versions of the same virus will permanently populate similar anatomic sites. Moreover, clinical reactivations of both vaccine varicella zoster virus (VZV) and wild-type VZV continue to occur [4, 5]. It is unknown to what extent these reactivations reflect waning immunity or the appearance of novel viral subtypes unrecognizable by existing immunologic defenses [6]. Shingles in young, otherwise healthy individuals cannot be explained on the basis of immunosenescence. More importantly, it is unknown how these 2 distinct viruses interact over time, particularly in hosts who later become immunocompromised. Zostavax is contraindicated in most patients who previously received Varivax. Nonimmune persons should receive Varivax, not Zostavax, but lack of immunity was not an exclusionary criterion in this trial [1].

The levels of circulating anti-VZV antibodies and their prevalence are already high in this population, and the incidence of herpes zoster (HZ) is lower than in older age groups. Periodic fluctuations in anti-VZV antibody levels due to subclinical reactivations of latent VZV may stimulate immunologic memory [7] in the absence of exogenous reexposure. Following natural infections, antibodies to VZV persist for long periods, with a half-life of around 50 years [7]. Yet, the durability of cell-mediated immunity is perhaps more crucial [8]. Although HZ may be severe, it is usually a self-limited, readily recognized, nonfatal clinical entity that responds to treatment with available antiviral agents even in seriously immunocompromised hosts.

Unfortunately, the influence of Zostavax on other serious complications of latent VZV such as meningoencephalitis, encephalitis, myelitis, angiopathy, and ophthalmologic infections [9] has not been adequately evaluated. Headache was the most frequent serious adverse event but no information is provided regarding its etiology [1]. Because this study focused on shingles, other virus-induced complications like zoster sine herpete may have been missed, which is comparable to HZ and postherpetic neuralgia for establishing vaccine efficacy. The confirmation of HZ cases centered on detection of VZV DNA by polymerase chain reaction (PCR) in specimens from skin lesions. On the basis of this test, less than half (129 of 277) of atypical cases of suspected HZ were actually confirmed as HZ. One is left wondering what caused the other 148 cases of suspected HZ. Herpes simplex DNA by PCR was also performed but no positive results were reported. Patients with clinical VZV disease may have false-negative tests for VZV DNA by PCR [10], which would result in an underestimation of HZ cases.

In addition, average follow-up in this study was only 1.3 years. No Hispanics were included, and white women, all from developed nations, were overrepresented. Long-term follow-up of Zostavax recipients is prudent and necessary. Further attenuation of the Oka strain of VZV to render it incapable of establishing latency could result in a safer vaccine, particularly for immunocompromised patients. However, in the greater scheme of public health and cost-effectiveness [11], Zostavax should remain a low priority.

Note

Potential conflicts of interest. Author certifies no potential conflicts of interest.

The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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