A varicella-zoster virus vaccine reduced the burden of illness of herpes zoster in older adults


In persons ≥60 years of age, does a live attenuated varicella-zoster virus (VZV) vaccine decrease the burden of illness caused by herpes zoster and the incidence of postherpetic neuralgia?

**METHODS**

Design: randomised placebo controlled trial (Shingles Prevention Study).

Allocation: (concealed)†.

Blinding: blinded (clinicians, participants, data collectors, outcome assessors, data analysts, and data safety and monitoring committee)†.

Follow-up period: mean 3.13 years.

Setting: 22 sites in the US.

Participants: 38 546 persons ≥60 years of age (median age 69 y, 59% men) who had a history of varicella or had lived in the US ≥30 years. Immunocompromised persons were excluded.

Intervention: 1 subcutaneous injection of 0.5 ml of Oka/Merck VZV vaccine (n = 19 270), or placebo (n = 19 276). The vaccine had median estimated potency of 24 600 plaque forming units.

Outcomes: vaccine efficacy with respect to the severity of illness caused by herpes zoster, defined as the relative reduction in burden of illness score (VEBOI) based on the severity of herpes zoster pain and its duration, comparing the vaccine and placebo groups. For the vaccine to be considered a success, the VEBOI point estimate had to be ≥47% with the lower limit of the 95% CI > 25%. The secondary outcome was vaccine efficacy with respect to the incidence of post-herpetic neuralgia (VEPHN) defined as pain rated as ≥3 (scale ranged from 0–10 [pain as bad as you can imagine]). The vaccine was considered a success if the VEPHN point estimate was ≥62% with a 95% CI lower limit > 25%.

Patient follow up: 95% (modified intention to treat analysis).

*See glossary.
†Information provided by author.

**MAIN RESULTS**

315 participants in the vaccine group and 642 in the placebo group developed herpes zoster. The incidence of herpes zoster was lower in participants who received the vaccine than in those who received placebo (score 2.21 v 5.68, 61% reduction, p<0.001). The results were not affected when stratified by sex or age. 27 participants in the vaccine group and 80 in the placebo group developed post-herpetic neuralgia (table); the results were not affected by sex or age.

**CONCLUSIONS**

In persons ≥60 years of age, a live attenuated varicella zoster virus vaccine decreased the burden of illness caused by herpes zoster and the incidence of post-herpetic neuralgia. The vaccine reduced the incidence of herpes zoster.

Abstract and commentary also appear in ACP Journal Club.

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**Commentary**

The study by Oxman et al may be the first to look at a vaccination strategy to prevent expression of a disease caused by reactivation of a latent infection acquired decades earlier. While zoster is seldom fatal, morbidity from post-herpetic neuralgia can be high, and the disease requires physician visits and prescriptions for antiviral drugs and analgesics. In persons with previous varicella, zoster can occur at any time, although risk increases with age (especially after 60 y). The participants in this study (immunocompetent adults ≥60 y) seem representative with a rate of zoster (among placebo recipients) similar to that previously described in a population based study. A single dose of vaccine substantially reduced the risk of herpes zoster (by 51%) and post-herpetic neuralgia (by 67%) over the 5.5 years of the double blinded study. Given that vaccination caused very few adverse events, the vaccine seems to be both safe and effective. Cost effectiveness will depend on the price of the vaccine and the costs of various outcomes (which have not yet been analysed). However, if the vaccine is available to the target population at a price comparable to that of the paediatric vaccine, a strong case could be made for administering it universally without regard to patient specific risk factors because the cost of treating zoster and its sequelae can be substantial. The biggest caveat would be for immunocompromised adults because neither safety nor efficacy has been measured yet in such patients. Encouragingly, the paediatric vaccine has been fairly safe in children with moderate immune deficiency.

For this new vaccine, the optimal age at first administration still needs to be determined. The duration of protection is unknown. While the relatively high NNT of 59 may seem unappealing, a vaccine with 100% protection against zoster would still have an NNT of 30.

Thomas Fekete, MD
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**Varicella-zoster vaccine (VZV) v placebo to prevent herpes zoster at mean 3.13 years**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Incidence per 1000 person-years</th>
<th>NNT (95% CI)</th>
<th>Vaccine efficacy (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VZV vaccine</td>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>Incidence of herpes zoster</td>
<td>5.42</td>
<td>11.12</td>
<td>59 (30 to 72)</td>
</tr>
<tr>
<td>Incidence of post-herpetic neuralgia</td>
<td>0.46</td>
<td>1.38</td>
<td>364 (259 to 577)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; NNT and CI calculated from number of confirmed cases of herpes zoster and post-herpetic neuralgia in article.*